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=> fil reg
FILE 'REGISTRY' E      ) AT 13:58:00 ON 28 OCT 2004
USE IS SUBJECT TO      TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP       TERMS" FOR DETAILS.
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Property values t      with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UP      27 OCT 2004  HIGHEST RN 770693-70-4
DICTIONARY FILE U      S:  27 OCT 2004  HIGHEST RN 770693-70-4

TSCA INFORMATION       URRENT THROUGH MAY 21, 2004

  Please note tha      rch-term pricing does apply when
  conducting Smar      CT searches.

Crossover limits       been increased.  See HELP CROSSOVER for details.

Experimental and       lated property data are now available. For more
information enter      PROP at an arrow prompt in the file or refer
to the file summa      eet on the web at:
http://www.cas.org     INE/DBSS/registryss.html

=> d que stat l3
L2                 STR
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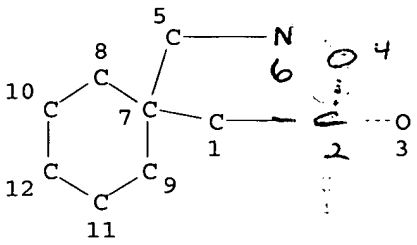


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS      ATOM
DEFAULT ECLEVEL IS     LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATE    OR EMBEDDED
NUMBER OF NODES IS

STEREO ATTRIBUTES:     NONE
L3             26 SEA      FILE=REGISTRY FAM FUL L2

100.0% PROCESSED       ITERATIONS                    26 ANSWERS
SEARCH TIME: 00.00

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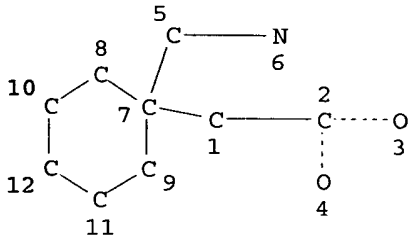

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

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L8         29686 SEA FILE=REGISTRY ABB=ON  PLU=ON  110-16-7/CRN
L9             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  50853-52-6/CRN
L10            0 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 AND (L7 OR L8 OR L9)
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=> fil caplus
FILE 'CAPLUS' ENTERED AT 13:58:19 ON 28 OCT 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 28 Oct 2004  VOL 141 ISS 18
FILE LAST UPDATED: 27 Oct 2004  (20041027/ED)
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This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

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L2             STR
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L4             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "TARTARIC ACID"/CN
L5             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "MALEIC ACID"/CN
L6             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  "ETHANEDISULFONIC ACID"/CN
L11          975 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3
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L13        1018 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 OR GABAPENTIN/OBI
L14       43984 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 OR L5 OR L6 OR (TARTARIC/OBI
                 OR MALEIC/OBI OR ETHANEDISULFONIC/OBI) (2W) ACID#/OBI
L15           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L13 AND L14
L16           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L15 OR L12
L21           2 SEA FILE=REGISTRY ABB=ON  PLU=ON  "D-TARTARIC ACID"/CN
L22           2 SEA FILE=REGISTRY ABB=ON  PLU=ON  "L-TARTARIC ACID"/CN
L23           2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L21 OR L22
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L17             9 SEA FILE=CAPLUS ABB=ON  PLU=ON  L13 (L) SALT#/OBI
L28            38 SEA FILE=CAPLUS ABB=ON  PLU=ON  L13 AND SALT?/OBI
L29             6 SEA FILE=CAPLUS ABB=ON  PLU=ON  L28 AND ACID SALT#/OBI
L30            11 SEA FILE=CAPLUS ABB=ON  PLU=ON  L29 OR L17


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L27  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:        2003:376842  CAPLUS
DOCUMENT NUMBER:         138:385297
TITLE:                   Methods for treating depression and other CNS
                         disorders using enantiomerically enriched desmethyl-
                         and didesmethyl- metabolites of citalopram
INVENTOR(S):             Bush, Larry R.; Currie, Mark G.; Senanayake, Chris H.;
                         Fang, Kevin Q.
PATENT ASSIGNEE(S):      Sepracor, Inc., USA
SOURCE:                  PCT Int. Appl., 58 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
     ---------------      ----   --------    --------------------   --------
     WO 2003040121         A1    20030515    WO 2002-US35408        20021105
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
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             NE, SN, TD, TG
     EP 1446396            A1    20040818    EP 2002-802848         20021105
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     BR 2002013949         A     20040831    BR 2002-13949          20021105
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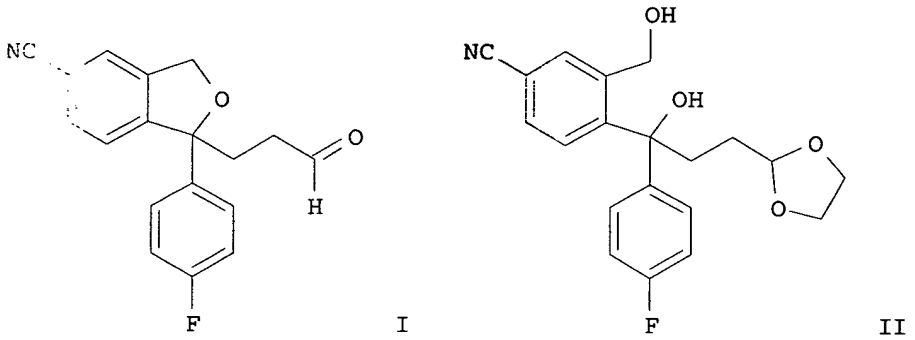
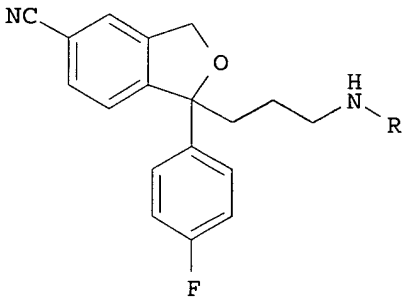
PRIORITY APPLN. INFO.: US 2001-337608P P 20011108
WO 2002-US35404 W 20021105

GI



I II



III

AB This invention relates to the preparation of I and II and derivs. of I and II in their racemic, enantiomerically enriched, or optically pure forms. This invention further relates to novel compns. of matter containing enantiomerically enriched (-)-desmethylcitalopram (-)-III (R = Me), (+)-didesmethylcitalopram (+)-III (R = Me), or (-)-didesmethylcitalopram (-)-III (R = H) or mixts. thereof in optimal ratios. Contrary to prior teachings, the enantiomerically enriched citalopram metabolites disclosed herein possess potent serotonin reuptake inhibitory activity, with minimal inhibitory effects on the reuptake of other known monoamines, e.g., norepinephrine (NE) or dopamine (DA). For example, stepwise reaction of 1-oxo-1,3-dihydroisobenzofuran-5-carbonitrile with 4-fluorophenylmagnesium bromide and the chiral Grignard reagent, which was prepared from 2-(2-bromoethyl)-[1,3]dioxolane and Mg powder, in THF gave II. Cyclization using mesyl chloride in CH2Cl2, followed by reduction provided the I. Reaction of the aldehyde with (-)-tert-butylsulfinamide in the presence of Ti(OEt)4 in EtOH afforded the sulfinamide, which was reduced to the amine III (R = H) with 10% HCl in MeOH. Protection of the amine with BOC anhydride in the presence of TEA in CH2Cl2 provided the enantiomerically enriched isomers, which were separated on a chiral column and subsequently deprotected with TFA to give (+)-III (R = H) and (-)-III (R = H). In biol. assays, (-)-III (R = H) and (+)-III (R = H) strongly inhibited serotonergic 5-HT receptor activity with Ki values of 5.8 nM and 90 nM, resp., with little effect on NE and DA transporter activity. By comparison, racemic citalopram inhibited serotonin reuptake with a Ki of 3.9 nM. The present invention also discloses methods for treating

disorders, dysfunctions and diseases for which inhibition of serotonin reuptake is therapeutically beneficial. In particular, the present invention discloses a method for treating various forms of depression and other CNS disorders with pharmaceutical compns. described herein.

IC ICM C07D307-87
ICS C07D317-20; A61K031-343; A61P025-00

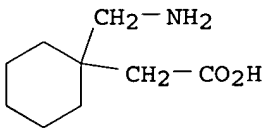
CC 27-7 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

IT 50-12-4, Mephenytoin 50-48-6, Amitriptyline 50-49-7, Imipramine 58-55-9, Theophylline, biological studies 81-81-2, Warfarin 90-39-1, Sparteine 298-46-4, Carbamazepine 5786-21-0, Clozapine 28911-01-5, Triazolam **60142-96-3**, **Gabapentin** 84057-84-1, Lamotrigine 106266-06-2, Risperidone
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy agent; preparation of enantiomerically enriched desmethyl- and didesmethyl- metabolites of citalopram for treating depression and other CNS disorders)

IT **87-69-4**, L-**Tartaric acid**, reactions
147-71-7, D-**Tartaric acid** 352-13-6, 4-Fluorophenylmagnesium bromide 18742-02-4, 2-(2-Bromoethyl)-[1,3]dioxolane 20580-80-7 24424-99-5, BOC anhydride 82104-74-3, 1-Oxo-1,3-dihydroisobenzofuran-5-carbonitrile 526204-40-0 526204-41-1 526204-44-4, (S)-1-(4-Fluorophenyl)-1-(3-oxopropyl)-1,3-dihydroisobenzofuran-5-carbonitrile
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of enantiomerically enriched desmethyl- and didesmethyl- metabolites of citalopram for treating depression and other CNS disorders)

IT **60142-96-3**, **Gabapentin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy agent; preparation of enantiomerically enriched desmethyl- and didesmethyl- metabolites of citalopram for treating depression and other CNS disorders)

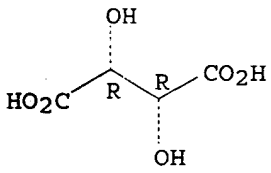
RN 60142-96-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



IT **87-69-4**, L-**Tartaric acid**, reactions
147-71-7, D-**Tartaric acid**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of enantiomerically enriched desmethyl- and didesmethyl- metabolites of citalopram for treating depression and other CNS disorders)

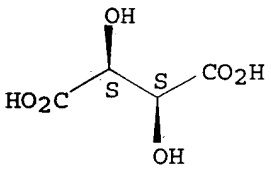
RN 87-69-4 CAPLUS
CN Butanedioic acid, 2,3-dihydroxy- (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 147-71-7 CAPLUS
CN Butanedioic acid, 2,3-dihydroxy-, (2S,3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:833023 CAPLUS
DOCUMENT NUMBER: 135:376738
TITLE: Compounds and methods for modulating cerebral amyloid angiopathy using inhibitors of an amyloid β peptide
INVENTOR(S): Green, Allan M.; Gervais, Francine
PATENT ASSIGNEE(S): Neurochem, Inc., Can.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085093	A2	20011115	WO 2000-IB2078	20001222
WO 2001085093	A3	20020829		
WO 2001085093	C2	20020926		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001084313	A5	20011120	AU 2001-84313	20001222
EP 1251837	A2	20021030	EP 2000-993855	20001222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2000016652	A	20021119	BR 2000-16652	20001222
US 2003003141	A1	20030102	US 2000-747408	20001222

US 6670399 B2 20031230
JP 2003532656 T2 20031105 JP 2001-581748 20001222
PRIORITY APPLN. INFO.: US 1999-171877P P 19991223
WO 2000-IB2078 W 20001222

OTHER SOURCE(S): MARPAT 135:376738

AB The invention provides methods of inhibiting cerebral amyloid angiopathy (CAA) and treating a disease state characterized by cerebral amyloid angiopathy, e.g., Alzheimer's disease, in a subject using an inhibitor of the 39-40 amino acid amyloid β peptide (Aβ40). The Aβ40 inhibitor is selected from, e.g., sulfonic acid derivs., such as ethanesulfonic acid, 1,2-ethanedisulfonic acid, 1-propanesulfonic acid, 1,3-propanedisulfonic acid, 1,4-butanedisulfonic acid, 1,5-pentanedisulfonic acid, 2-aminoethanesulfonic acid, 4-hydroxy-1-butanesulfonic acid, 1-butanesulfonic acid, 1-decanesulfonic acid, 2-propanesulfonic acid, 3-pentanesulfonic acid, 4-heptanesulfonic acid, etc., and pharmaceutically acceptable salts thereof or from from phosphonic acid derivs., such as diethylphosphonoacetic acid, phenylphosphonic acid, 3-aminopropylphosphonic acid, propylphosphonic acid, etc. The compds. are formulated in a dispersion system, a liposome formulation, or microspheres using a polymeric matrix. The polymeric matrix is selected from natural polymers, such as albumin, alginate, cellulose derivs., collagen, fibrin, gelatin, and polysaccharides, or synthetic polymers such as polyesters, polyethylene glycol, poloxamers, and polyanhydrides. For example, the ability of compds. of the invention to inhibit CAA was measured in 9 wk old hAPP transgenic mice treated with two different concns. of a compound of the present invention, 3-amino-1-propanesulfonic acid sodium salt, 100 and 30 mg/kg. Mice were administered the compound for 8 wk, after which they were sacrificed and their brains were perfused and processed for histol. staining with Thioflavin S. This method may also be used as a screening method for determining activity of a candidate compound for inhibiting CAA. The extent of CAA in brain sections obtained from these animals was qual. determined following staining. The results indicate that the test compound was effective in (i) reducing the number of mice showing CAA, and (ii) showing an effect on the severity of the deposition seen in the brain vasculature of these animals.

IC ICM A61K
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT 81-08-3 107-35-7, 2-Aminoethanesulfonic acid **110-04-3**, 1,2-**Ethanedisulfonic acid** 116-63-2 149-45-1 288-94-8, 1H-Tetrazole 594-45-6 Ethanesulfonic acid 831-59-4 860-22-0 926-39-6 993-13-5, Methylphosphonic acid 1068-21-9, Diethyl phosphoramidate 1071-83-6, N-Phosphonomethylglycine 1120-71-4 1132-61-2, 4-Morpholinepropanesulfonic acid 1135-40-6 1571-33-1, Phenylphosphonic acid 1633-83-6 2386-47-2, 1-Butanesulfonic acid 2386-54-1 3095-95-2, Diethylphosphonoacetic acid 3687-18-1, 3-Amino-1-propanesulfonic acid 4408-78-0, Phosphonoacetic acid 4426-50-0 4672-38-2, Propylphosphonic acid 4923-84-6 5117-07-7 5284-66-2, 1-Propanesulfonic acid 5399-58-6 5652-28-8 5994-73-0 6779-09-5, Ethylphosphonic acid 7365-45-9 13138-33-5, 3-Aminopropylphosphonic acid 13419-61-9 13991-98-5 14047-23-5, (1-Aminopropyl)phosphonic acid 14159-48-9, 2-Propanesulfonic acid 14650-46-5 15471-17-7 15763-57-2 18039-42-4 20283-21-0, 1-Decanesulfonic acid 21668-77-9, 1,3-Propanedisulfonic acid 23052-80-4 23052-81-5 25331-57-1 25595-59-9 26978-64-3, 4-Hydroxy-1-butanesulfonic acid 27665-39-0, 1,4-Butanedisulfonic acid 27797-35-9 31465-25-5 34159-44-9 36585-99-6 37810-68-7 38911-09-0 40391-99-9 40465-65-4, N-Phosphonomethylglycine trisodium salt 51224-03-4 51224-04-5 51650-30-7, 3-Pentanesulfonic acid

51762-95-9 53329-36-5 57605-13-7 58849-79-9 **60142-96-3**
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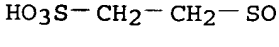
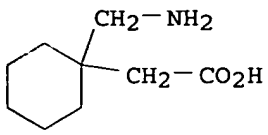
373645-13-7 373645-14-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of amyloid β peptide for modulating cerebral amyloid angiopathy)

IT **110-04-3**, 1,2-**Ethanedisulfonic acid**
60142-96-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of amyloid β peptide for modulating cerebral amyloid angiopathy)

RN 110-04-3 CAPLUS
CN 1,2-Ethanedisulfonic acid (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 60142-96-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



L27 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:693017 CAPLUS
DOCUMENT NUMBER: 135:256625
TITLE: Composition and method to treat weight gain and obesity attributable to psychotropic drugs
INVENTOR(S): Wurtman, Judith J.; Wurtman, Richard J.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001067890	A2	20010920	WO 2001-US6637	20010302
WO 2001067890	A3	20020207		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-525058 A2 20000314

AB A composition and method of use for the prevention and/or treatment of weight problems attributed to the use of psychotropic drugs contains at least one form of carbohydrate and is substantially free of protein. In a preferred embodiment the composition is in the form of a snack food. Administration of the snack food results in an elevation of the subject's plasma Tp/Lnaa ratio, relative to the subject's pre-administration plasma Tp/Lnaa (tryptophan/large neutral amino acids) ratio. In alternative embodiments, the snack food either further contains tryptophan, 5-hydroxytryptophan, or melatonin, or is administered either after, concurrently, or before the administration of a second composition that contains either tryptophan, 5-hydroxytryptophan or melatonin.

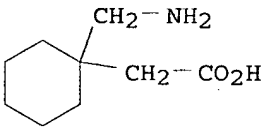
IC ICM A23L001-09
ICS A23L001-29
CC 18-4 (Animal Nutrition)
Section cross-reference(s): 17
IT 50-36-2, Cocaine 298-46-4, Tegretal 298-59-9, Ritalin 549-18-8, Elavil 16676-29-2, Trexan 17321-77-6, Anafranil 28981-97-7, Xanax 56296-78-7, Prozac **60142-96-3**, Neurontin 76584-70-8, Depakote 79559-97-0, Zoloft 99300-78-4 106266-06-2, Risperdal
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(composition and method to treat weight gain and obesity attributable to psychotropic drugs)

IT 50-21-5, Lactic acid, biological studies 50-67-9, Serotonin, biological studies 50-67-9D, Serotonin, salts 50-81-7, Ascorbic acid, biological studies 50-99-7, Dextrose, biological studies 57-50-1, Sucrose, biological studies 59-23-4, D-Galactose, biological studies 63-42-3, Lactose 64-19-7, Acetic acid, biological studies 69-79-4, Maltose 73-22-3, L-Tryptophan, biological studies 73-31-4, Melatonin 77-92-9, Citric acid, biological studies **87-69-4, Tartaric acid**, biological studies 110-15-6, Succinic acid, biological studies 110-17-8, Fumaric acid, biological studies 124-04-9, Adipic acid, biological studies 3458-28-4, D-Mannose 4350-09-8, 5-Hydroxytryptophan 6915-15-7, Malic acid 9004-53-9, Dextrin 9005-25-8, Starch, biological studies 9050-36-6, Maltodextrin
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition and method to treat weight gain and obesity attributable to psychotropic drugs)

IT **60142-96-3**, Neurontin
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(composition and method to treat weight gain and obesity attributable to psychotropic drugs)

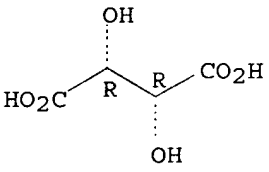
RN 60142-96-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



IT **87-69-4, Tartaric acid**, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition and method to treat weight gain and obesity attributable to psychotropic drugs)

RN 87-69-4 CAPLUS
CN Butanedioic acid, 2,3-dihydroxy- (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L27 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:725436 CAPLUS
DOCUMENT NUMBER: 133:301171
TITLE: Compositions and methods for improved delivery of ionizable hydrophobic therapeutic agents
INVENTOR(S): Chen, Feng-jing; Patel, Manesh V.

PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059475	A1	20001012	WO 2000-US7342	20000316
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6383471	B1	20020507	US 1999-287043	19990406
EP 1165048	A1	20020102	EP 2000-916547	20000316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-287043 A 19990406
WO 2000-US7342 W 20000316

AB The present invention is directed to a pharmaceutical composition including a hydrophobic therapeutic agent having at least one ionizable functional group, and a carrier. The carrier includes an ionizing agent capable of ionizing the functional group, a surfactant, and optionally solubilizers, triglycerides, and neutralizing agents. The invention further relates to a method of preparing such compns. by providing a composition of an ionizable hydrophobic therapeutic agent, an ionizing agent, and a surfactant, and neutralizing a portion of the ionizing agent with a neutralizing agent. The compns. of the invention are particularly suitable for use in oral dosage forms. A carrier containing concentrated phosphoric acid 0.025, Tween-20 0.3, Arlacel 186 0.2, sodium taurocholate 0.15, propylene glycol 0.3 g was formulated. Itraconazole was included in the carrier at 30 mg/mL for testing the stability of the itraconazole solution upon dilution in simulated gastric fluid.

IC ICM A61K009-14
ICS A61K009-48; A61K009-64; A61K009-66; A01N025-00

CC 63-6 (Pharmaceuticals)

IT 50-06-6, Phenobarbital, biological studies 50-21-5, biological studies 50-21-5D, Lactic acid, glycerides 50-44-2, Mercaptopurine 50-48-6, Amitriptyline 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies 50-55-5, Reserpine 50-78-2 50-81-7, Ascorbic acid, biological studies 51-48-9, Levothyroxine, biological studies 51-52-5, Propylthiouracil 51-55-8, Atropine, biological studies 51-64-9, Dexamphetamine 52-86-8, Haloperidol 53-86-1, Indomethacin 54-05-7, Chloroquine 54-11-5, Nicotine 54-31-9 56-54-2, Quinidine 57-10-3, Palmitic acid, biological studies 57-11-4, Stearic acid, biological studies 57-22-7, Vincristine 57-27-2, Morphine, biological studies 57-41-0, Phenytoin 57-43-2, Amylobarbital 57-44-3, Barbital 57-47-6, Physostigmine 57-66-9, Probenecid 57-88-5, Cholesterol, biological studies 58-14-0, Pyrimethamine 58-25-3, Chlordiazepoxide 58-32-2, Dipyridamole 58-38-8, Prochlorperazine 58-39-9, Perphenazine 58-54-8, Ethacrynic acid 58-73-1, Diphenhydramine 58-94-6, Chlorothiazide 59-05-2, Methotrexate 59-66-5, Acetazolamide 59-87-0,

Nitrofurazone 59-96-1, Phenoxybenzamine 61-56-3, Sulthiame 61-68-7, Mefenamic acid 61-72-3, Cloxacillin 64-18-6, Formic acid, biological studies 64-19-7, Acetic acid, biological studies 64-77-7, Tolbutamide 65-85-0, Benzoic acid, biological studies 66-76-2, Dicumarol 66-79-5, Oxacillin 67-20-9, Nitrofurantoin 68-04-2, Sodium Citrate 68-11-1, Thioglycolic acid, biological studies 68-35-9, Sulfadiazine 69-23-8, Fluphenazine 69-72-7, biological studies 69-93-2, Uric acid, biological studies 72-44-6, Methaqualone 72-69-5, Nortriptyline 74-55-5, Ethambutol 75-75-2, Methanesulfonic acid 76-57-3, Codeine 76-74-4, Pentobarbital 76-99-3, Methadone 77-28-1, Butobarbital 77-36-1, Chlorthalidone 77-86-1, Tromethamine 77-92-9, biological studies 79-09-4, Propanoic acid, biological studies 79-10-7, Acrylic acid, biological studies 82-92-8, Cyclizine 83-68-1, Vitamin K6 83-69-2, Vitamin K7 83-70-5, Vitamin K5 83-89-6, Mepacrine 86-21-5, Pheniramine 86-22-6, Brompheniramine 86-35-1, Ethotoin 86-42-0, Amodiaquine **87-69-4**, biological studies 89-57-6, Mesalamine 89-65-6, Isoascorbic acid 90-82-4, Pseudoephedrine 90-84-6, Diethylpropion 94-20-2, Chlorpropamide 97-23-4, Dichlorophen 99-66-1, Valproic acid 101-31-5, Hyoscyamine 102-71-6, biological studies 104-15-4, p-Toluenesulfonic acid, biological studies 107-15-3, 1,2-Ethanediamine, biological studies 107-92-6, Butyric acid, biological studies 110-15-6, Butanedioic acid, biological studies **110-16-7**, 2-Butenedioic acid (2Z)-, biological studies 110-17-8, Fumaric acid, biological studies 110-27-0, Isopropyl myristate 111-03-5, Glyceryl monooleate 111-62-6, Ethyl Oleate 111-90-0, Transcutol 112-80-1, Oleic acid, biological studies 113-15-5, Ergotamine 113-45-1, Methylphenidate 113-59-7, Chlorprothixene 113-92-8 114-07-8, Erythromycin 115-38-8, Methylphenobarbital 117-89-5, Trifluoperazine 121-44-8, biological studies 122-09-8, Phentermine 122-20-3, Triisopropanolamine 124-04-9, Hexanedioic acid, biological studies 125-28-0, Dihydrocodeine 125-53-1, Oxyphencyclimine 125-84-8, Aminoglutethimide 127-09-3, Sodium Acetate 127-33-3, Demeclocycline 127-69-5, Sulfafurazole 127-71-9, Sulfabenzamide 127-79-7, Sulfamerazine 128-13-2, Ursodeoxycholic acid 128-37-0, Butylated Hydroxytoluene, biological studies 129-03-3, Cyproheptadine 129-20-4, Oxyphenbutazone 130-95-0, Quinine 132-17-2, Benztropine 138-36-3, p-Bromophenylsulfonic acid 139-33-3, Edetate Disodium 141-43-5, biological studies 142-18-7, Glyceryl monolaurate 142-91-6, Isopropyl palmitate 143-07-7, Lauric acid, biological studies 144-11-6, Benzhexol 144-55-8, Sodium hydrogen carbonate, biological studies 144-62-7, Ethanedioic acid, biological studies 144-80-9, Sulfacetamide 144-83-2, Sulfapyridine 145-42-6, Taurocholic acid, sodium salt 146-22-5, Nitrazepam 146-54-3, Fluopromazine 148-79-8, Thiabendazole 151-21-3, Sodium Dodecyl Sulfate, biological studies 154-42-7, Thioguanine 190-39-6, Bisanthene 288-14-2, Isoxazole 298-57-7, Cinnarizine 299-42-3, Ephedrine 300-62-9, Amphetamine 302-79-4, Tretinoin 305-03-3, Chlorambucil 321-64-2, Tacrine 359-83-1, Pentazocine 361-37-5, Methysergide 364-62-5, Metoclopramide 389-08-2 396-01-0, Triamterene 404-86-4, Capsaicin 437-38-7, Fentanyl 439-14-5, Diazepam 442-52-4, Clemizole 443-48-1, Metronidazole 446-86-6, Azathioprine 458-24-2, Fenfluramine 463-79-6, Carbonic acid, biological studies 471-34-1, Calcium carbonate, biological studies 486-16-8, Carbinoxamine 500-92-5, Proguanil 511-12-6, Dihydroergotamine 514-65-8, Biperiden 519-23-3, Ellipticine 522-00-9, Ethopropazine 523-87-5, Dimenhydrinate 525-66-6 526-95-4, D-Gluconic acid 536-33-4, Ethionamide 537-21-3, Chlorproguanil 544-35-4, Ethyl linoleate 544-63-8, Myristic acid, biological studies 548-73-2, Droperidol 561-27-3, Diamorphine 564-25-0, Doxycycline 569-65-3, Meclozine 577-11-7, Docusate sodium 599-79-1, Sulfasalazine 603-50-9, Bisacodyl 604-75-1, Oxazepam 631-61-8, Ammonium Acetate

644-62-2, Meclofenamic acid 657-24-9, Metformin 668-94-0, 4,5-Diphenylimidazole 671-16-9, Procarbazine 723-46-6, Sulfamethoxazole 738-70-5, Trimethoprim 739-71-9, Trimipramine 745-65-3, Alprostadil 768-94-5, Amantadine 846-49-1, Lorazepam 846-50-4, Temazepam 848-75-9, Lormetazepam 865-21-4, Vinblastine 911-45-5, Clomiphene 915-30-0, Diphenoxylate 961-71-7, Phenbenzamine 968-81-0, Acetohexamide 1134-47-0, Baclofen 1156-19-0, Tolazamide 1309-42-8, Magnesium hydroxide 1310-58-3, Potassium Hydroxide, biological studies 1310-73-2, Sodium Hydroxide, biological studies 1327-43-1, Magnesium aluminum silicate 1330-80-9, Propylene glycol oleate 1333-28-4, Undecenoic acid 1335-30-4, Aluminum silicate 1336-21-6, Ammonium Hydroxide 1338-39-2, Sorbitan monolaurate 1338-41-6, Sorbitan monostearate 1338-43-8, Sorbitan monooleate 1400-61-9, Nystatin 1404-90-6, Vancomycin 1406-05-9, Penicillin 1508-75-4, Tropicamide 1553-60-2, Ibufenac 1622-61-3, Clonazepam 1622-62-4, Flunitrazepam 1812-30-2, Bromazepam 1951-25-3, Amiodarone 1972-08-3, Dronabinol 2022-85-7, Flucytosine 2030-63-9, Clofazimine 2062-78-4, Pimozide 2078-54-8, Propofol 2447-57-6, Sulfadoxine 2487-39-0, Vitamin K-S (II) 2515-61-9, 1,5-Diphenylpyrazoline 2609-46-3, Amiloride 2709-56-0, Flupentixol 2898-12-6, Medazepam 2998-57-4, Estramustine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing hydrophobic therapeutic agents and carriers containing ionizing agents and surfactants and triglycerides)

IT 3056-17-5, Stavudine 3116-76-5, Dicloxacillin 3239-44-9, Dexfenfluramine 3737-09-5, Disopyramide 4117-33-3, Lysine Ethyl Ester 4342-03-4, Dacarbazine 4759-48-2, Isotretinoin 5002-47-1, Fluphenazine decanoate 5036-02-2, Tetramisole 5051-62-7, Guanabenz 5104-49-4, Flurbiprofen 5306-85-4, Dimethyl Isosorbide 5588-33-0, Mesoridazine 5633-20-5, Oxybutynin 5786-21-0, Clozapine 6452-71-7, Oxprenolol 6493-05-6, Pentoxifylline 6506-37-2, Nimorazole 7087-68-5, Diisopropylethylamine 7261-97-4, Dantrolene 7416-34-4, Molindone 7647-01-0, Hydrochloric Acid, biological studies 7664-38-2, Phosphoric acid, biological studies 7664-38-2D, Phosphoric acid, esters, biological studies 7664-93-9, Sulfuric acid, biological studies 7681-93-8, Natamycin 7689-03-4, Camptothecin 7697-37-2, Nitric acid, biological studies 7778-53-2, Potassium Phosphate 8007-43-0, Sorbitan sesquioleate 8045-34-9, Pentaerythritol stearate 9002-92-0, Polyoxyethylene lauryl ether 9002-93-1 9002-96-4, D-α-Tocopheryl polyethylene glycol succinate 9004-74-4, Methoxy polyethylene glycol 9004-95-9, Polyethylene glycol cetyl ether 9004-98-2, Polyoxyethylene oleyl ether 9004-99-3, Myrj 51 9005-00-9, Polyoxyethylene stearyl ether 9005-08-7, Polyethylene glycol distearate 9005-32-7, Alginic acid 9005-64-5, Polysorbate 20 9005-65-6, Polysorbate 80 9005-66-7, Tween 40 9005-67-8, Tween 60 9007-48-1, Polyglyceryl oleate 9011-21-6 9011-29-4 9014-67-9, Aloxiprin 9016-45-9 9062-73-1, Polyethylene glycol sorbitan laurate 9062-90-2, Polyethylene glycol sorbitan oleate 10034-85-2, Hydriodic acid 10035-10-6, Hydrobromic acid, biological studies 10043-35-3, Boric acid, biological studies 10238-21-8 10262-69-8, Maprotiline 10457-90-6, Bromperidol 10540-29-1, Tamoxifen 11140-04-8, Imwitor 988 12633-72-6, Amphotericin 12772-47-3, Pentaerythritol oleate 13292-46-1, Rifampin 13392-28-4, Rimantadine 13523-86-9 13655-52-2, Alprenolol 14028-44-5, Amoxapine 14611-51-9, Selegiline 14808-79-8, Sulfate, biological studies 15307-86-5, Diclofenac 15574-96-6, Pizotifen 15676-16-1, Sulpiride 15686-51-8, Clemastine 15686-71-2, Cephalexin 15686-83-6, Pyrantel 15687-27-1, Ibuprofen 16110-51-3, Cromoglicic acid 16773-42-5, Ornidazole 17560-51-9, Metolazone 17617-23-1, Flurazepam 18016-80-3, Lysuride 18507-89-6, Decoquinate 18559-94-9, Albuterol 19216-56-9, Prazosin 19387-91-8, Tinidazole 19794-93-5, Trazodone 20594-83-6,

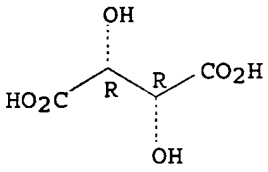
Nalbuphine 21187-98-4, Gliclazide 21256-18-8, Oxaprozin 21645-51-2, Aluminum hydroxide, biological studies 21738-42-1, Oxamniquine 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 22131-79-9, Alclofenac 22204-53-1 22232-71-9, Mazindol 22494-42-4, Diflunisal 22882-95-7, Isopropyl linoleate 22916-47-8, Miconazole 22994-85-0, Benznidazole 23031-25-6, Terbutaline 23110-15-8, Fumagillin 23288-49-5, Probucol 23593-75-1, Clotrimazole 24219-97-4, Mianserin 25339-99-5, Sucrose monolaurate 25523-97-1, Dexchlorpheniramine 25614-03-3, Bromocriptine 25637-84-7, Glyceryl dioleate 25637-97-2, Sucrose dipalmitate 25812-30-0, Gemfibrozil 25953-19-9, Cefazolin 26097-80-3, Cambendazole 26171-23-3, Tolmetin 26266-57-9, Sorbitan monopalmitate 26266-58-0, Sorbitan trioleate 26402-22-2, Glyceryl monocaprate 26402-26-6, Glyceryl monocaprylate 26446-38-8, Sucrose monopalmitate 26658-19-5, Sorbitan tristearate 26839-75-8, Timolol 26912-41-4D, Polyethylene glycol caprate, glycerides 27195-16-0, Sucrose distearate 27203-92-5, Tramadol 27220-47-9, Econazole 27321-96-6, Polyethylene glycol cholesterol 27638-00-2, Glyceryl dilaurate 28395-03-1, Bumetanide 28657-80-9, Cinoxacin 28911-01-5, Triazolam 28981-97-7, Alprazolam 29094-61-9, Glipizide 29122-68-7, Atenolol 29679-58-1, Fenoprofen 29767-20-2, Teniposide 30299-08-2, Clinofibrate 30909-51-4, Flupentixol decanoate 31431-39-7, Mebendazole 31692-85-0, Glycofurol 33419-42-0, Etoposide 33671-46-4, Clotiazepam 33940-98-6 34406-66-1, Nikkol Decaglyn 1L 34580-13-7, Ketotifen 34911-55-2, Bupropion 36322-90-4, Piroxicam 36330-85-5, Fenbufen 36354-80-0, Glyceryl dicaprylate 36531-26-7, Oxantel 36894-69-6, Labetalol 37148-27-9, Clenbuterol 37220-82-9, ARLACEL 186 37318-31-3, Crodesta F-160 37321-62-3, Lauroglycol FCC 37517-30-9, Acebutolol 38194-50-2, Sulindac 38304-91-5, Minoxidil 38821-53-3, Cephradine 39366-43-3, Magnesium aluminum hydroxide 41340-25-4, Etodolac 41859-67-0, Bezafibrate 42200-33-9, Nadolol 42399-41-7, Diltiazem 42766-91-6, Nikkol DHC 43200-80-2, Zopiclone 43210-67-9, Fenbendazole 50679-08-8, Terfenadine 51192-09-7, Nikkol TMGO 5 51264-14-3, Amsacrine 51322-75-9, Tizanidine 51384-51-1, Metoprolol 51481-61-9, Cimetidine 51803-78-2 51938-44-4, Sorbitan sesquistearate 52081-33-1, Mitomycins 52468-60-7, Flunarizine 52504-24-2, Softigen 767 52581-71-2, Volpo 3 52942-31-1, Etoperidone 53168-42-6, Myvacet 9-45 53179-11-6, Loperamide 53230-10-7, Mefloquine 53716-50-0, Oxfendazole 53988-07-1, Glyceryl dicaprate 54029-12-8, Ricobendazole 54143-55-4, Flecainide 54340-58-8, Meptazinol 54392-26-6, Sorbitan monoisostearate 54910-89-3, Fluoxetine 55142-85-3, Ticlopidine 55268-74-1, Praziquantel 55985-32-5, Nicardipine 57107-95-6 57307-93-4, Pentaerythritol caprylate 57801-81-7, Brotizolam 57808-66-9, Domperidone 58581-89-8, Azelastine 59467-70-8, Midazolam 59729-33-8, Citalopram **60142-96-3**, **Gabapentin** 60607-34-3, Oxatomide 60719-84-8, Amrinone 61318-90-9, Sulconazole 61379-65-5, Rifapentine 61869-08-7 62013-04-1, Dirithromycin 62571-86-2, Captopril 63590-64-7, Terazosin 63675-72-9, Nisoldipine 64211-45-6, Oxiconazole 64221-86-9, Imipenem 64840-90-0, Eperisone 64872-76-0, Butoconazole 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 65899-73-2, Tioconazole 66085-59-4, Nimodipine 66357-35-5, Ranitidine 67227-56-9, Fenoldopam 67352-02-7 67915-31-5, Terconazole 68506-86-5, Vigabatrin 68844-77-9, Astemizole 68958-64-5, Polyethylene glycol glyceryl trioleate 68993-42-0D, Polyethylene glycol caprylate, glycerides 69070-98-0 69756-53-2, Halofantrine 70458-96-7, Norfloxacin 71125-38-7, Meloxicam 71486-22-1, Vinorelbine 72432-03-2, Miglitol 72509-76-3, Felodipine 72559-06-9, Rifabutin 72803-02-2, Darodipine 73590-58-6, Omeprazole 74011-58-8, Enoxacin 74103-06-3, Ketorolac 74191-85-8, Doxazosin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing hydrophobic therapeutic agents and

carriers containing ionizing agents and surfactants and triglycerides)

IT **87-69-4**, biological studies **110-16-7**, 2-Butenedioic acid (2Z)-, biological studies **60142-96-3**, **Gabapentin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing hydrophobic therapeutic agents and carriers containing ionizing agents and surfactants and triglycerides)

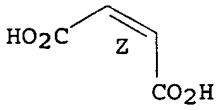
RN 87-69-4 CAPLUS
CN Butanedioic acid, 2,3-dihydroxy- (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

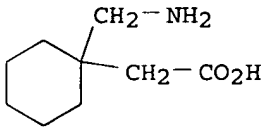


RN 110-16-7 CAPLUS
CN 2-Butenedioic acid (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 60142-96-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:608551 CAPLUS
DOCUMENT NUMBER: 133:213151
TITLE: Pharmaceutical compositions and methods for improved delivery of hydrophobic therapeutic agents
INVENTOR(S): Patel, Manesh V.; Chen, Feng-Jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000050007		A1	20000831	WO 2000-US165	20000105
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6294192		B1	20010925	US 1999-258654	19990226
AU 2000022242		A5	20000914	AU 2000-22242	20000105
AU 771659		B2	20040401		
EP 1158959		A1	20011205	EP 2000-901394	20000105
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537317		T2	20021105	JP 2000-600619	20000105
NZ 513810		A	20040227	NZ 2000-513810	20000105
PRIORITY APPLN. INFO.:				US 1999-258654 A	19990226
				WO 2000-US165 W	20000105

AB The present invention relates to triglyceride-free pharmaceutical compns. for delivery of hydrophobic therapeutic agents. Compns. of the present invention include a hydrophobic therapeutic agent and a carrier, where the carrier is formed from a combination of a hydrophilic surfactant and a hydrophobic surfactant. Upon dilution with an aqueous solvent, the composition forms
a clear, aqueous dispersion of the surfactants containing the therapeutic agent.
The invention also provides methods of treatment with hydrophobic therapeutic agents using these compns. A pharmaceutical composition contained cyclosporin 0.14, Cremophor RH-40 0.41, Arlacel186 0.29, sodium taurocholate 0.26, and propylene glycol 0.46 mg.

IC ICM A61K009-127
ICS A61K009-107; A61K038-13

CC 63-6 (Pharmaceuticals)

IT 50-14-6, Ergocalciferol 50-21-5D, Lactic acid, glycerides 50-24-8, Prednisolone 50-28-2, EStradiol, biological studies 50-70-4, Sorbitol, biological studies 51-48-9, L-Thyroxine, biological studies 52-01-7, Spironolactone 55-98-1, Busulphan 56-81-5, 1,2,3-Propanetriol, biological studies 56-81-5D, Glycerol, polyethylene fatty acid esters 57-10-3, Hexadecanoic acid, biological studies 57-11-4, Octadecanoic acid, biological studies 57-55-6, 1,2-Propanediol, biological studies 57-55-6D, Propylene glycol, ethers 57-83-0, Progesterone, biological studies 57-88-5, Cholesterol, biological studies 57-88-5D, Cholesterol, polyoxyethylene derivs. 60-33-3, 9,12-Octadecadienoic acid (9Z,12Z)-, biological studies 64-17-5, Ethanol, biological studies 66-76-2, Dicoumarol 67-20-9, Nitrofurantoin 67-45-8, Furazolidone 67-63-0, Isopropanol, biological studies 67-96-9, Dihydrotachysterol 67-97-0, Cholecalciferol 69-65-8, Mannitol 71-36-3, Butanol, biological studies 76-57-3, Codeine 76-99-3, Methadone 77-89-4, Acetyl triethylcitrate 77-90-7, Acetyl tributyl citrate 77-92-9D, Citric acid, diglycerides 77-93-0, Triethylcitrate 77-94-1, Tributylcitrate 81-24-3 81-25-4 83-44-3 87-33-2, Isosorbide dinitrate **87-69-4D, Tartaric acid,** glycerides, biological studies 90-82-4, Pseudoephedrine 100-51-6, Benzenemethanol, biological studies 102-76-1, Triacetin 104-31-4, Benzonatate 105-37-3, EThyl propionate 105-54-4, Ethyl butyrate 105-60-2, biological studies 105-60-2D, Caprolactam, N-Alkyl derivs. 106-32-1, Ethyl caprylate 107-21-1, 1,2-Ethanediol, biological studies 110-27-0, Isopropyl myristate 111-03-5, Glyceryl monooleate 111-62-6,

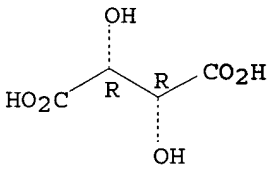
Crodamol EO 111-90-0, Transcutol 112-80-1, 9-Octadecenoic acid (9Z)-, biological studies 113-15-5, Ergotamine 113-92-8, Chlorpheniramine 115-77-5, biological studies 115-83-3, Pentaerythrityl Tetra stearate 124-07-2, Octanoic acid, biological studies 125-84-8, Aminoglutethimide 126-07-8, Griseofulvin 127-19-5, Dimethylacetamide 128-13-2 141-22-0 142-18-7, Glyceryl monolaurate 142-62-1, Hexanoic acid, biological studies 142-91-6, Isopropyl palmitate 143-07-7, Dodecanoic acid, biological studies 151-41-7, Lauryl sulfate 155-97-5, Pyridostigmine 298-46-4, 5H-Dibenz[b,f]azepine-5-carboxamide 298-57-7, Cinnarizine 298-81-7, Methoxsalen 300-62-9, Amphetamine 302-79-4, Tretinoin 303-49-1, Clomipramine 321-64-2, Tacrine 334-48-5, Decanoic acid 359-83-1, Pentazocine 360-65-6 378-44-9, Betamethasone 404-86-4, Capsaicin 437-38-7, Fentanyl 443-48-1, Metronidazole 463-40-1 474-25-9 475-31-0 511-12-6, Dihydroergotamine 516-35-8 516-50-7 520-85-4, Medroxyprogesterone 542-28-9, δ-Valerolactone 544-35-4, Ethyl linoleate 544-63-8, Tetradecanoic acid, biological studies 577-11-7, Sodium docusate 595-33-5 616-45-5, Pyrrolidone 616-45-5D, Pyrrolidone, N-Alkyl derivs. 623-84-7, Propylene glycol diacetate 640-79-9 675-20-7, 2-Piperidone 872-50-4, N-Methylpyrrolidone, biological studies 1134-47-0, Baclofen 1331-12-0, Propylene glycol monoacetate 1335-71-3, Propylene glycol oleate 1338-39-2, Arlacel 20 1338-43-8, Span 80 1397-89-3, Amphotericin B 1406-16-2, Vitamin D 1406-18-4, Vitamin E 1951-25-3, Amiodarone 1972-08-3, Tetrahydrocannabinol 2687-91-4, N-Ethylpyrrolidone 2687-94-7 2687-96-9 3068-88-0, β-Butyrolactone 3445-11-2 4419-39-0, BeclomethAsone 4759-48-2, Isotretinoin 5104-49-4, Flurbiprofen 5306-85-4, Dimethyl isosorbide 7261-97-4, Dantrolene 7488-99-5, α Carotene 7664-93-9D, Sulfuric acid, salts alkyl derivs., biological studies 7689-03-4, Camptothecin 8007-43-0, Sorbitan sesquioleate 9002-89-5, Polyvinylalcohol 9002-92-0, Brij 30 9002-96-4 9003-39-8, Polyvinylpyrrolidone 9004-65-3, Hydroxypropyl methylcellulose 9004-74-4, Methoxy polyethylene glycol 9004-81-3, Polyoxyethylene laurate 9004-95-9, Polyoxyethylene cetyl ether 9004-96-0, PEG-32 oleate 9004-98-2, Polyoxyethylene oleyl ether 9004-99-3, Polyoxyethylene stearate 9005-00-9, Polyoxyethylene stearyl ether 9005-02-1, Polyoxyethylene dilaurate 9005-07-6, Polyoxyethylene dioleate 9005-08-7, Polyoxyethylene distearate 9005-32-7D, Alginic acid, salts 9005-37-2, Propylene glycol alginate 9005-63-4D, Polyoxyethylene sorbitan, derivs. 9005-63-4D, Polyoxyethylene sorbitan, fatty acid esters 9005-64-5, Tween 20 9005-65-6, Polysorbate 80 9005-66-7, Tween 40 9005-67-8, Tween 60 9007-48-1, PLUROLOLEIQUECC497 9011-21-6, Polyoxyethylene glyceryl stearate 9016-45-9 9036-19-5 10238-21-8, Glyburide 10540-29-1, Tamoxifen 11103-57-4, Vitamin A 11140-04-8, Imwitor 988 12001-79-5, Vitamin K 12619-70-4, Cyclodextrin 12619-70-4D, Cyclodextrin, derivs. 12619-70-4D, Cyclodextrin, hydroxypropyl ethers 13081-97-5, Pentaerythrityl di stearate 14440-80-3, Stearoyl-2-lactylate 14605-22-2 15307-86-5, Diclofenac 15574-96-6, Pizotifen 15686-51-8, Clemastine 15687-27-1, Ibuprofen 18559-94-9, Albuterol 19356-17-3, Calcifediol 20594-83-6, Nalbuphine 20830-75-5, Digoxin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22882-95-7, Isopropyl linoleate 22916-47-8, Miconazole 23288-49-5, Probucol 25168-73-4, Sucrose monostearate 25265-75-2, Butanediol 25322-68-3 25322-69-4, Polypropylene glycol 25339-99-5, Sucrose monolaurate 25523-97-1, Dexchlorpheniramine 25618-55-7D, Polyglycerol, fatty acid esters 25637-84-7, Glyceryl dioleate 25637-97-2, Sucrose dipalmitate 25812-30-0, Gemfibrozil 26266-57-9, Sorbitan monopalmitate 26266-58-0, Sorbitan Trioleate 26402-22-2, Glyceryl monocaprate 26402-26-6, Glyceryl monocaprylate 26446-38-8, Sucrose monopalmitate 27154-43-4D, Piperidone, N-Alkyl derivs. 27195-16-0, Sucrose distearate 27203-92-5, TRamadol 27638-00-2, Glyceryl dilaurate 29094-61-9,

Glipizide 29767-20-2, Teniposide 31692-85-0, Glycofurol 32222-06-3, Calcitriol 33069-62-4, Paclitaxel 33419-42-0, Etoposide 34911-55-2, Bupropion 36354-80-0, Glyceryl dicaprylate 37321-62-3, Lauroglycol 38304-91-5, Minoxidil 41340-25-4, Etodolac 42924-53-8, Nabumetone 43200-80-2, Zopiclone 49562-28-9, Fenofibrate 49697-38-3, Rimexolone 51333-22-3, Budesonide 51481-61-9, Cimetidine 51938-44-4, Sorbitan sesquistearate 52581-71-2, Volpo 3 53123-88-9, Sirolimus 53168-42-6, Myvacet 9-45 53179-11-6, Loperamide 53230-10-7, Mefloquine 53988-07-1, Glyceryl dicaprate 54392-26-6, Sorbitan monoisostearate 54965-21-8, Albendazole 55079-83-9, Acitretin 55142-85-3, Ticlopidine 57107-97-8, Polyoxyethylene glyceryl oleate 59467-70-8, Midazolam 59865-13-3, Cyclosporine **60142-96-3, Gabapentin** 61379-65-5, Rifapentine 61869-08-7 62013-04-1, Dirithromycin 62356-64-3 63590-64-7, Terazosin 63612-50-0, Nilutamide 63675-72-9, Nisoldipine 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 68506-86-5, Vigabatrin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. and methods for improved delivery of hydrophobic therapeutic agents)

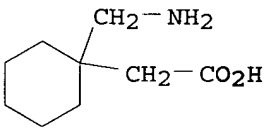
IT **87-69-4D, Tartaric acid**, glycerides, biological studies **60142-96-3, Gabapentin**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. and methods for improved delivery of hydrophobic therapeutic agents)

RN 87-69-4 CAPLUS
CN Butanedioic acid, 2,3-dihydroxy- (2R,3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 60142-96-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:832438 CAPLUS
DOCUMENT NUMBER: 141:297645
TITLE: A process for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its acid addition **salt** by

neutralization with base
INVENTOR(S): Gurunath, Gaonkar Subhash; Rajamannar, Thennati; Shrivastava, Ratnesh
PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Ltd., India
SOURCE: Indian, 10 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 186285	A	20010728	IN 2000-MU76	20000124

PRIORITY APPLN. INFO.: IN 2000-MU76 20000124

AB A process is described for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid (i.e., gabapentin) from an aqueous solution containing acid addition salt of 1-(aminomethyl)cyclohexaneacetic acid [e.g., 1-(aminomethyl)cyclohexaneacetic acid hydrochloride] by treatment with a base (e.g., sodium hydroxide) to the isoelec. point. The process yields pure 1-(aminomethyl)cyclohexaneacetic acid directly from the aqueous solution containing its acid addition salt, which salt is generated during the synthesis of 1-(aminomethyl)cyclohexaneacetic acid by the acid hydrolysis of its corresponding lactam.

IC ICM C07C175-00

CC 45-4 (Industrial Organic Chemicals, Leather, Fats, and Waxes)
Section cross-reference(s): 24, 48

ST **gabapentin** prepn aminomethylcyclohexaneacetic acid hydrochloride **salt** neutralization sodium hydroxide; aminomethylcyclohexaneacetic mineral **acid salt**

IT Hydrolysis
(acid; of 1-(aminomethyl)cyclohexaneacetic acid lactam with mineral acid into 1-(aminomethyl)cyclohexaneacetic acid mineral **acid salts**)

IT **Salts**, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(of 1-(aminomethyl)cyclohexaneacetic acid; process for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its acid addition **salt** by neutralization with base)

IT Neutralization
(process for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its acid addition **salt** by neutralization with base)

IT Alkali metal hydroxides
Bases, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its acid addition **salt** by neutralization with base)

IT Amines, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(**salts**, 1-(aminomethyl)cyclohexaneacetic acid mineral **acid salts**; process for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its acid addition **salt** by neutralization with base)

IT 497-19-8, Sodium carbonate, reactions 534-17-8, Cesium carbonate 554-13-2, Lithium carbonate 584-08-7, Potassium carbonate 1305-62-0, Calcium hydroxide, reactions 1309-42-8, Magnesium hydroxide 1310-58-3, Potassium hydroxide, reactions 1310-65-2, Lithium hydroxide 1310-73-2, Sodium hydroxide, reactions 17194-00-2, Barium hydroxide 21351-79-1,

Cesium hydroxide
RL: RCT (Reactant); RACT (Reactant or reagent)
(base; process for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its **acid** addition **salt** by neutralization with base)

IT **60142-96-3P, Gabapentin**
RL: IMF (Industrial manufacture); PREP (Preparation)
(process for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its acid addition **salt** by neutralization with base)

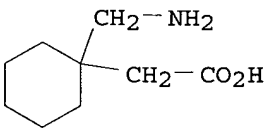
IT **60142-95-2P, Gabapentin** hydrochloride
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); **RACT** (Reactant or reagent)
(process for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its acid addition **salt** by neutralization with base)

IT 64744-50-9, **Gabapentin** lactam **585540-04-1**
585540-05-2 585540-06-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its acid addition **salt** by neutralization with base)

IT 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; process for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its **acid** addition **salt** by neutralization with base)

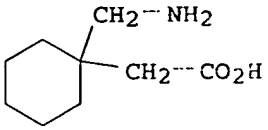
IT **60142-96-3P, Gabapentin**
RL: IMF (Industrial manufacture); PREP (Preparation)
(process for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its acid addition **salt** by neutralization with base)

RN 60142-96-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



IT **60142-95-2P, Gabapentin** hydrochloride
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); **RACT** (Reactant or reagent)
(process for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its acid addition **salt** by neutralization with base)

RN 60142-95-2 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)

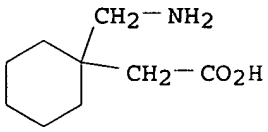


IT **585540-04-1 585540-05-2 585540-06-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the isolation of pure 1-(aminomethyl)cyclohexaneacetic acid from an aqueous solution of its acid addition salt by neutralization with base)

RN 585540-04-1 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)-, sulfate (1:1) (9CI) (CA INDEX NAME)

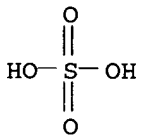
CM 1

CRN 60142-96-3
CMF C9 H17 N O2



CM 2

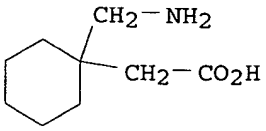
CRN 7664-93-9
CMF H2 O4 S



RN 585540-05-2 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)-, phosphate (1:1) (9CI) (CA INDEX NAME)

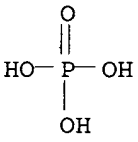
CM 1

CRN 60142-96-3
CMF C9 H17 N O2



CM 2

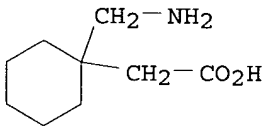
CRN 7664-38-2
CMF H3 O4 P



RN 585540-06-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)-, **nitrate** (9CI) (CA INDEX NAME)

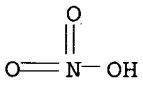
CM 1

CRN 60142-96-3
CMF C9 H17 N O2



CM 2

CRN 7697-37-2
CMF H N O3



L30 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:803929 CAPLUS
DOCUMENT NUMBER: 141:301482
TITLE: Phenolic **acid salts** of **gabapentin** in liquid **and/or** semi-solid dosage forms and methods of use
INVENTOR(S): Kiel, Jeffrey S.; Thomas, H. Greg; Mani, Narasimhan
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004192618	A1	20040930	US 2004-806260	20040322
PRIORITY APPLN. INFO.:			US 2003-457408P P	20030325

AB The present invention relates to pharmaceutical compns. of gabapentin tannate, processes for production of those compns. and methods of use of those compns. The present invention provides a novel process for preparation of the tannate salt of gabapentin in liquid or semi-solid dosage form for human and veterinary pharmaceutical use. Tannate salts of active pharmaceutical ingredients are used in sustained release applications and to improve certain organoleptic properties such as taste. The process may utilize either natural or synthetic tannic acid.

IC ICM C07H005-04
ICS A61K031-7024
NCL 514023000; 536018700
CC 63-6 (Pharmaceuticals)
ST **gabapentin** tannate prepn
IT Drug delivery systems
(carriers; phenolic **acid salts** of **gabapentin** in liquid and/or semi-solid dosage forms)
IT Nervous system, disease
(central; phenolic **acid salts** of **gabapentin** in liquid and/or semi-solid dosage forms)
IT Drug delivery systems
(liqs., dispersions; phenolic **acid salts** of **gabapentin** in liquid and/or semi-solid dosage forms)
IT Drug delivery systems
(liqs.; phenolic **acid salts** of **gabapentin** in liquid and/or semi-solid dosage forms)
IT Acacia
Agglomeration preventers
Buffers
Dispersing agents
Flavoring materials
Human
Nervous system agents
Preservatives
Solvents
Sweetening agents
Thickening agents
pH
(phenolic **acid salts** of **gabapentin** in liquid and/or semi-solid dosage forms)
IT Kaolin, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phenolic **acid salts** of **gabapentin** in liquid and/or semi-solid dosage forms)
IT Tannins
RL: RCT (Reactant); RACT (Reactant or reagent)
(phenolic **acid salts** of **gabapentin** in liquid and/or semi-solid dosage forms)
IT Tannins
RL: RCT (Reactant); RACT (Reactant or reagent)

(salts with gabapentin; phenolic acid salts of gabapentin in liquid and/or semi-solid dosage forms)

IT Drug delivery systems
(solids; phenolic acid salts of gabapentin in liquid and/or semi-solid dosage forms)

IT Paraffin oils
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; phenolic acid salts of gabapentin in liquid and/or semi-solid dosage forms)

IT 57-50-1, Sucrose, biological studies 94-13-3, Propylparaben 94-26-8, Butylparaben 99-76-3, Methylparaben 128-44-9, Saccharin sodium 1327-43-1, Magnesium aluminum silicate 9000-65-1, Tragacanth 9000-69-5, Pectin 9004-34-6D, Cellulose, derivs. 11138-66-2, Xanthan gum 22839-47-0, Aspartame 56038-13-2, Sucralose
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phenolic acid salts of gabapentin in liquid and/or semi-solid dosage forms)

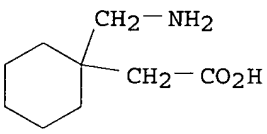
IT **60142-96-3**, Gabapentin
RL: RCT (Reactant); RACT (Reactant or reagent)
(phenolic acid salts of gabapentin in liquid and/or semi-solid dosage forms)

IT **60142-96-3DP**, Gabapentin, tannate salts
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phenolic acid salts of gabapentin in liquid and/or semi-solid dosage forms)

IT 56-81-5, Glycerin, uses 57-55-6, Propylene glycol, uses 64-17-5, Ethanol, uses 67-63-0, Isopropanol, uses 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; phenolic acid salts of gabapentin in liquid and/or semi-solid dosage forms)

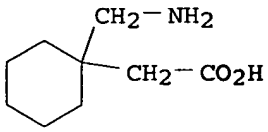
IT **60142-96-3**, Gabapentin
RL: RCT (Reactant); RACT (Reactant or reagent)
(phenolic acid salts of gabapentin in liquid and/or semi-solid dosage forms)

RN 60142-96-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



IT **60142-96-3DP**, Gabapentin, tannate salts
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phenolic acid salts of gabapentin in liquid and/or semi-solid dosage forms)

RN 60142-96-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)

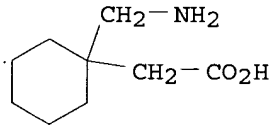


L30 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:803928 CAPLUS
DOCUMENT NUMBER: 141:301481
TITLE: Process for preparing phenolic **acid salts** of **gabapentin**
INVENTOR(S): Kiel, Jeffrey S.; Thomas, H. Greg; Mani, Narasimhan
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

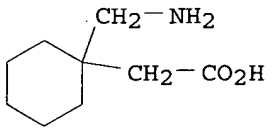
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004192617	A1	20040930	US 2004-806022	20040322
PRIORITY APPLN. INFO.:			US 2003-457431P P	20030325

AB The present invention provides a novel process for preparation of the tannate salt of gabapentin for human and veterinary pharmaceutical use. Tannate salts of active pharmaceutical ingredients are used in sustained release applications and to improve certain organoleptic properties such as taste. However, the prior art neither discloses nor suggests the preparation of gabapentin tannate. The process for preparing gabapentin tannate includes the mixing of gabapentin and tannic acid together in the presence of one or more solvents. The method may further include the step of selecting the one or more solvents from a group consisting of purified water, ethanol, glycerin, propylene glycol, diethylether, methylene chloride, acetone, iso-Pr alc. and mixts. thereof. The process may also include the steps of isolating and purifying the tannate salt. This may be accomplished by filtration, drying, centrifugation and lyophilization. The process may utilize either natural or synthetic tannic acid.
IC ICM A61K031-7024
ICS A61K031-195
NCL 514023000; 514561000
CC 63-6 (Pharmaceuticals)
ST **gabapentin** tannate prepn
IT Tannins
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**gabapentin salts**; process for preparing phenolic **acid salts** of **gabapentin**)
IT Centrifugation
Freeze drying
Human
Solvents
(process for preparing phenolic **acid salts** of **gabapentin**)
IT Tannins
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparing phenolic **acid salts** of

gabapentin)
IT Drug delivery systems
(sustained-release; process for preparing phenolic **acid salts** of **gabapentin**)
IT 67-63-0, Isopropyl alcohol, uses 67-64-1, Acetone, uses 75-09-2, Methylene chloride, uses
RL: NUU (Other use, unclassified); USES (Uses)
(process for preparing phenolic **acid salts** of **gabapentin**)
IT **60142-96-3, Gabapentin**
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparing phenolic **acid salts** of **gabapentin**)
IT **60142-96-3DP, Gabapentin**, tannate **salts**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for preparing phenolic **acid salts** of **gabapentin**)
IT 56-81-5, Glycerin, uses 57-55-6, Propylene glycol, uses 60-29-7, Diethylether, uses 64-17-5, Ethanol, uses 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; process for preparing phenolic **acid** salts of **gabapentin**)
IT **60142-96-3, Gabapentin**
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparing phenolic **acid salts** of **gabapentin**)
RN 60142-96-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



IT **60142-96-3DP, Gabapentin**, tannate **salts**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for preparing phenolic **acid salts** of **gabapentin**)
RN 60142-96-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



L30 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:803927 CAPLUS
DOCUMENT NUMBER: 141:301480
TITLE: Phenolic **acid salts** of **gabapentin** in solid dosage forms and methods

of use
INVENTOR(S): Kiel, Jeffrey S.; Thomas, H. Greg; Mani, Narasimhan
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004192616	A1	20040930	US 2004-805806	20040322
PRIORITY APPLN. INFO.:			US 2003-457399P	P 20030325

AB The present invention relates to pharmaceutical compns. of gabapentin tannate in solid dosage form, processes for production of those compns. and methods of use of those compns. Tannate salts of active pharmaceutical ingredients are used in sustained release applications and to improve certain organoleptic properties such as taste. The process may utilize either natural or synthetic tannic acid.

IC ICM A61K031-7024
ICS A61K031-195
NCL 514023000; 514561000
CC 63-6 (Pharmaceuticals)
ST **gabapentin** tannate prepn tablet
IT Drug delivery systems
(capsules; phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)
IT Drug delivery systems
(carriers; phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)
IT Nervous system, disease
(central; phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)
IT Tannins
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**gabapentin salts**; phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)
IT Drug delivery systems
(oral; phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)
IT Lubricants
(pharmaceutical; phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)
IT Binders
Fillers
Nervous system agents
Sweetening agents
(phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)
IT Tannins
RL: RCT (Reactant); RACT (Reactant or reagent)
(phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)
IT Hydrocarbon oils
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)

IT Drug delivery systems
(tablets; phenolic acid **salts** of **gabapentin** in solid dosage forms and methods of use)

IT 57-11-4, Stearic acid, biological studies 57-50-1, Sucrose, biological studies 63-42-3, Lactose 69-65-8, Mannitol 557-04-0, Magnesium stearate 1327-43-1, Magnesium aluminum silicate 1592-23-0, Calcium stearate 9003-39-8, Polyvinylpyrrolidone 9004-34-6, Cellulose, derivs. 11138-66-2, Xanthan gum 14807-96-6, Talc, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticlumping agent; phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)

IT 7631-86-9, Silica, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(colloidal, anticlumping agent; phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)

IT 128-44-9, Saccharin sodium 22839-47-0, Aspartame 56038-13-2, Sucralose
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)

IT **60142-96-3, Gabapentin**
RL: RCT (Reactant); RACT (Reactant or reagent)
(phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)

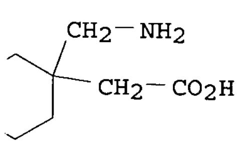
IT **60142-96-3DP, Gabapentin**, tannate **salts**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)

IT 56-81-5, Glycerin, uses 57-55-6, Propylene glycol, uses 64-17-5, Ethanol, uses 67-63-0, Isopropanol, uses 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; phenolic acid **salts** of **gabapentin** in solid dosage forms and methods of use)

IT **60142-96-3, Gabapentin**
RL: RCT (Reactant); RACT (Reactant or reagent)
(phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)

RN 60142-96-3 CAPLUS

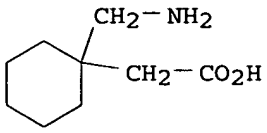
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



IT **60142-96-3DP, Gabapentin**, tannate **salts**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phenolic **acid salts** of **gabapentin** in solid dosage forms and methods of use)

RN 60142-96-3 CAPLUS

CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



L30 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:747816 CAPLUS
DOCUMENT NUMBER: 141:260286
TITLE: Process for the preparation of **gabapentin** free from inorganic acid anions by precipitation and neutralization of a **gabapentin** hydroxybenzoate **salt**
INVENTOR(S): Breviglieri, Gabriele; Contrini, Sergio; Assanelli, Cinzia
PATENT ASSIGNEE(S): Farchemia S.R.L., Italy
SOURCE: U.S., 3 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6790986	B1	20040914	US 2003-445676	20030527
EP 1468985	A1	20041020	EP 2004-8806	20040414

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

PRIORITY APPLN. INFO.: IT 2003-MI825 A 20030418

AB Gabapentin which is free of mineral acid anions is obtained by precipitating from a gabapentin aqueous solution a corresponding hydroxybenzoate (e.g., gabapentin salicylate), from which pure gabapentin is subsequently obtained by dissoln. in a lower alc. (e.g., ethanol) and neutralization with a tertiary base (e.g., ethyldiisopropylamine).

IC ICM C07C061-10
ICS A61K031-195
NCL 562507000; 514561000
CC 24-5 (Alicyclic Compounds)
Section cross-reference(s): 45, 63
ST **gabapentin** purifn hydroxybenzoate **salt** formation pptn base neutralization
IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(aryl, hydroxy, hydroxybenzoic acids; in a process for the preparation of **gabapentin** free from inorg. acid anions by precipitation and neutralization of a **gabapentin** hydroxybenzoate **salt**)
IT Drying
Neutralization
(in a process for the preparation of **gabapentin** free from inorg. acid anions by precipitation and neutralization of a **gabapentin** hydroxybenzoate **salt**)
IT Alcohols, uses
RL: NUU (Other use, unclassified); USES (Uses)
(lower, solvents; in a process for the preparation of **gabapentin** free from inorg. acid anions by precipitation and neutralization of a

gabapentin hydroxybenzoate **salt**)

IT Precipitation (chemical)
(process for the preparation of **gabapentin** free from inorg. acid anions by precipitation and neutralization of a **gabapentin** hydroxybenzoate **salt**)

IT Amines, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(tertiary, bases; in a process for the preparation of **gabapentin** free from inorg. acid anions by precipitation and neutralization of a **gabapentin** hydroxybenzoate **salt**)

IT 7087-68-5, Ethyldiisopropylamine
RL: RGT (Reagent); RACT (Reactant or reagent)
(base; in a process for the preparation of **gabapentin** free from inorg. acid anions by precipitation and neutralization of a **gabapentin** hydroxybenzoate **salt**)

IT **60142-96-3P, Gabapentin**
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); RCT (Reactant); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(process for the preparation of **gabapentin** free from inorg. acid anions by precipitation and neutralization of a **gabapentin** hydroxybenzoate **salt**)

IT **756486-04-1P 756486-05-2P**
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(process for the preparation of **gabapentin** free from inorg. acid anions by precipitation and neutralization of a **gabapentin** hydroxybenzoate **salt**)

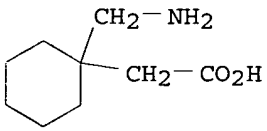
IT 69-72-7, Salicylic acid, reactions 99-96-7, 4-Hydroxybenzoic acid, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the preparation of **gabapentin** free from inorg. acid anions by precipitation and neutralization of a **gabapentin** hydroxybenzoate **salt**)

IT 64-17-5, Ethanol, uses 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; in a process for the preparation of **gabapentin** free from inorg. acid anions by precipitation and neutralization of a **gabapentin** hydroxybenzoate **salt**)

IT **60142-96-3P, Gabapentin**
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); RCT (Reactant); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(process for the preparation of **gabapentin** free from inorg. acid anions by precipitation and neutralization of a **gabapentin** hydroxybenzoate **salt**)

RN 60142-96-3 CAPLUS

CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



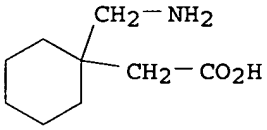
IT **756486-04-1P 756486-05-2P**
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical

process); PYP (Physical process); RCT (Reactant); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(process for the preparation of **gabapentin** free from inorg. acid anions by precipitation and neutralization of a **gabapentin** hydroxybenzoate salt)

RN 756486-04-1 CAPLUS
CN Benzoic acid, 2-hydroxy-, compd. with 1-(aminomethyl)cyclohexaneacetic acid (1:1) (9CI) (CA INDEX NAME)

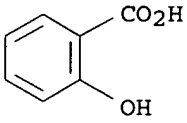
CM 1

CRN 60142-96-3
CMF C9 H17 N O2



CM 2

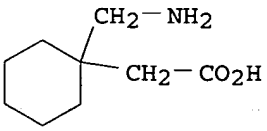
CRN 69-72-7
CMF C7 H6 O3



RN 756486-05-2 CAPLUS
CN Benzoic acid, 4-hydroxy-, compd. with 1-(aminomethyl)cyclohexaneacetic acid (1:1) (9CI) (CA INDEX NAME)

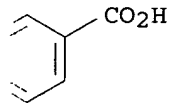
CM 1

CRN 60142-96-3
CMF C9 H17 N O2



CM 2

CRN 99-96-7
CMF C7 H6 O3



ENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 6 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
SION NUMBER: 2004:453163 CAPLUS
ENT NUMBER: 140:423949
: Improved process for preparation of gabapentin
TOR(S): Saigal, Jagdish Chand; Gupta, Rajender Pershad; Naik, Rajesh Vinodrai; Rajshekhar, Araddy; Joshi, Rajesh Dilip
T ASSIGNEE(S): Nicholas Piramal India Limited, India
E: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
ENT TYPE: Patent
AGE: English
Y ACC. NUM. COUNT: 1
T INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004046084	A1	20040603	WO 2002-IN221	20021118

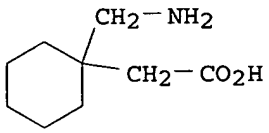
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

ITY APPLN. INFO.: WO 2002-IN221 20021118

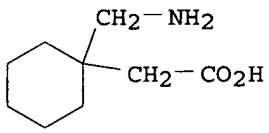
A process for producing gabapentin [1-(aminomethyl)-1-cyclohexaneacetic acid] from gabapentin hydrochloride salt involves conversion to gabapentin sulfate which is converted to free base using an inorg. base such as barium hydroxide.

ICM C07C227-42
34-2 (Amino Acids, Peptides, and Proteins)
gabapentin prepn neutralization **salt**
60142-96-3P, Gabapentin
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(production of **gabapentin** from its hydrochloride **salt**)
60142-95-2, Gabapentin hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(production of **gabapentin** from its hydrochloride **salt**)
1305-62-0, Calcium hydroxide, reactions 1310-58-3, Potassium hydroxide, reactions 1310-73-2, Sodium hydroxide, reactions 17194-00-2, Barium hydroxide
RL: RGT (Reagent); RACT (Reactant or reagent)
(production of **gabapentin** from its hydrochloride **salt**)
60142-96-3P, Gabapentin

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(production of **gabapentin** from its hydrochloride salt)
RN 60142-96-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



IT **60142-95-2**, **Gabapentin** hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(production of **gabapentin** from its hydrochloride salt)
RN 60142-95-2 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

L30 ANSWER 7 OF 11 **CAPLUS** COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:331964 CAPLUS
DOCUMENT NUMBER: 140:344917
TITLE: Gabapentin tablets preparation
INVENTOR(S): Manikandan, Ramalingam; Gogia, Ashish; Roy, Sunilendu Bhushan; Malik, Rajiv
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004032905	A1	20040422	WO 2003-IB4436	20031008
WO 2004032905	C1	20040610		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,

CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2002-DE1023 A 20021008

AB The present invention is generally directed to methods for preparing stable gabapentin tablets by wet granulation. A wet granulation method for preparing gabapentin tablets includes forming a mixture by dry mixing of a first portion of a binder with the gabapentin, one or more excipients, or a combination of the gabapentin and the one or more excipients; and adding a second portion of the binder to the mixture, wherein the second portion of the binder is in the form of a solution or dispersion.

IC ICM A61K009-20
ICS A61K031-195

CC 63-6 (Pharmaceuticals)

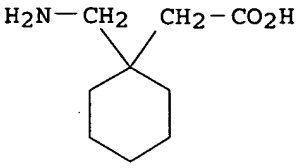
IT 9003-39-8, Pvp 9004-32-4, Carboxymethyl cellulose sodium salt 9004-34-6, Cellulose, biological studies 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hpmc 9063-38-1, Sodium starch glycolate 25086-89-9 106392-12-5, Poloxamer
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gabapentin tablets preparation)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:855904 CAPLUS
DOCUMENT NUMBER: 139:323791
TITLE: Synthesis and purification of gabapentin
INVENTOR(S): Bercovici, Sorin; Sasson, Sabar; Ulanenko, Konstantin
PATENT ASSIGNEE(S): Taro Pharmaceutical Industries Ltd., Israel; Taro Pharmaceuticals U.S.A., Inc.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003089403	A1	20031030	WO 2003-US11687	20030416
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004034248	A1	20040219	US 2003-414823	20030416

PRIORITY APPLN. INFO.: US 2002-373412P P 20020416
OTHER SOURCE(S): CASREACT 139:323791
GI



I

AB Synthesis and purification of gabapentin (I), by Hofmann rearrangement of 1-(2-amino-2-oxoethyl)-cyclohexaneacetic acid (II) and salt formation and ion exchange reactions, is claimed. Thus, II was reacted with NaOCl and NaOH in H2O to give I sodium salt, which was then suspended in 2-propanol and treated with HCl gas to produce the I HCl salt (III). Intermediate III in 2-propanol solution was then treated with Amberlite® IRA 67 for 2-3 h. until constant pH 8-8.5 was achieved, and the solution filtered. After work-up, I was isolated in 62% overall yield from starting II.

IC ICM C07C229-28
ICS C07C227-40; C07C227-42

CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 24, 63

ST Hofmann rearrangement hydrolysis redn alkali amine **salt** prepn **gabapentin**; ion exchange alkali amine **salt** purifn prepn **gabapentin**

IT Alkali metal **salts**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and purification of **gabapentin** using Hofmann rearrangement reaction)

IT Amines, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**salts**; preparation and purification of **gabapentin** using Hofmann rearrangement reaction)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:678769 CAPLUS
DOCUMENT NUMBER: 139:197197
TITLE: Preparation of new mineral acid addition **salts** of **gabapentin**
INVENTOR(S): Vittal, Tangirala Venkata Subramanya Krishna; Taj, Shabbir Ali; Kodimuthali, Armugam; Maddali, Kasturaiah
PATENT ASSIGNEE(S): Shasun Chemicals and Drugs Limited, India
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070683	A1	20030828	WO 2002-IN29	20020222

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,

RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2002-IN29 20020222

OTHER SOURCE(S): CASREACT 139:197197

AB A process for preparing mineral acid addition salts of gabapentin (e.g., gabapentin dihydrogen phosphate) comprises: (a) treating 1,1-cyclohexanediacetic acid monoamide with sodium hypobromite to effect a decarbonylation; (b) acidifying the reaction mass with a mineral acid (e.g., phosphoric acid) to a pH of about 2; (c) extracting the acid addition salt with a ketone solvent (e.g., MEK); (d) evaporating the solvent; (e) dissolving the extract in an alc. solvent (e.g., isopropanol); (f) filtering the undissolved material and evaporating the alc. solvent to obtain a syrupy residue; and (g) mixing the residue with non-polar organic solvents (e.g., toluene) to obtain mineral acid addition salts of gabapentin.

IC ICM C07C061-06

CC 24-5 (Alicyclic Compounds)
Section cross-reference(s): 45, 63

ST acid addn **salt gabapentin** prepn; **gabapentin** dihydrogen phosphate prepn

IT Amines, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(bases; in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT Carboxylic acids, uses
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(esters, solvents; in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT Hydrocarbons, uses
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(halo, solvents; in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT Crystallization
Filtration
(in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT Bases, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT Acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(inorg.; in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT Extraction
(liquid-liquid; in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT Decarbonylation
(of 1,1-cyclohexanediacetic acid monoamide with sodium hypobromite in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT Neutralization
(of **gabapentin** with mineral acids in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT Amines, preparation

RL: SPN (Synthetic preparation); PREP (Preparation)
(**salts**, mineral acid addition **salts** of **gabapentin**; **gabapentin** with mineral acids in the preparation of new mineral acid addition **salts of gabapentin**
)

IT Alcohols, uses
Aromatic hydrocarbons, uses
Ketones, uses
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(solvents; in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT 75-50-3, Trimethylamine, reactions 102-69-2, Tripropylamine 102-82-9, Tributylamine 102-86-3, Trihexylamine 121-44-8, Triethylamine, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(base; in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT 7664-38-2, Phosphoric acid, reactions 7664-93-9, Sulfuric acid, reactions 7697-37-2, Nitric acid, reactions 99189-60-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT 13824-96-9, Sodium hypobromite
RL: RGT (Reagent); RACT (Reactant or reagent)
(in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT **60142-96-3P, Gabapentin**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of anhydrous **gabapentin** form II from its mineral acid addition **salts**)

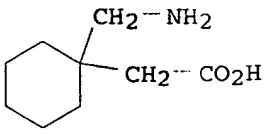
IT **585540-04-1P 585540-05-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of new mineral acid addition **salts of gabapentin**
)

IT **585540-06-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of new mineral acid addition **salts of gabapentin**
)

IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, 2-Propanol, uses 67-64-1, Acetone, uses 67-66-3, Trichloromethane, uses 71-23-8, 1-Propanol, uses 71-36-3, 1-Butanol, uses 71-43-2, Benzene, uses 75-09-2, Dichloromethane, uses 75-65-0, tert-Butanol, uses 78-92-2, 2-Butanol 78-93-3, MEK, uses 79-01-6, Trichloroethylene, uses 79-20-9, Methyl acetate 107-06-2, Ethylene dichloride, uses 108-10-1, MIBK 108-88-3, Methylbenzene, uses 141-78-6, Ethyl acetate, uses 563-80-4, Methyl isopropyl ketone
RL: NUU (Other use, unclassified); REM (Removal or disposal); PROC (Process); USES (Uses)
(solvent; in the preparation of new mineral acid addition **salts** of **gabapentin**)

IT **60142-96-3P, Gabapentin**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of anhydrous **gabapentin** form II from its mineral acid addition **salts**)

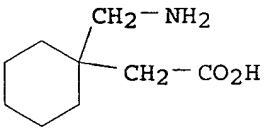
RN 60142-96-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



IT **585540-04-1P 585540-05-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of new mineral acid addition salts of gabapentin
)
RN 585540-04-1 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)-, sulfate (1:1) (9CI) (CA INDEX NAME)

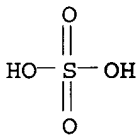
CM 1

CRN 60142-96-3
CMF C9 H17 N O2



CM 2

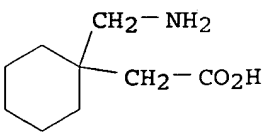
CRN 7664-93-9
CMF H2 O4 S



RN 585540-05-2 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)-, phosphate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 60142-96-3
CMF C9 H17 N O2



CM 2

CRN 7664-38-2
CMF H3 O4 P

)

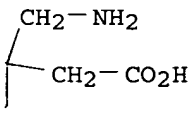
⟩—OH

)H

585540-06-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of new mineral acid addition **salts** of **gabapentin**
)
585540-06-3 CAPLUS
Cyclohexaneacetic acid, 1-(aminomethyl)-, nitrate (9CI) (CA INDEX NAME)

CM 1

CRN 60142-96-3
CMF C9 H17 N O2



CM 2

CRN 7697-37-2
CMF H N O3

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I—OH

RENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 10 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
SSION NUMBER: 2003:511118 CAPLUS
MENT NUMBER: 139:90451
E: Zero-order sustained-release dosage forms
NTOR(S): Heimlich, John M.; Noack, Robert M.; Cox, Steve R.; Ganorkar, Loksidh D.; Verhage, Ronald R.; John, Lee E.
NT ASSIGNEE(S): Pharmacia Corporation, USA
CE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
MENT TYPE: Patent
UAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053402	A1	20030703	WO 2002-US41104	20021219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003133982	A1	20030717	US 2002-324719	20021219
EP 1455751	A1	20040915	EP 2002-792508	20021219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.:
US 2001-342642P P 20011220
US 2001-342819P P 20011220
WO 2002-US41104 W 20021219

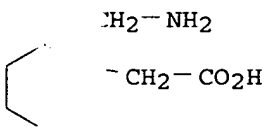
AB The present invention relates to zero-order sustained-release solid dosage forms suitable for administration of a wide range of drugs, especially those that are water-soluble The solid dosage form comprises (a) a matrix core comprising Et cellulose and the active agent and (b) a hydrophobic polymer coating encasing the entire matrix core. Thus, tablets contained clindamycin-HCl 76.44, Et cellulose 18.08, and Mg stearate 0.25%. Extra-granular formulations comprised Ethocel 4.99, and Mg stearate 0.25%. The coating composition comprised HPMC 10.8, and Surelease 43.2%.

IC ICM A61K009-00
CC 63-6 (Pharmaceuticals)
IT 50-48-6, Amitriptyline 50-70-4, Sorbitol, biological studies 50-99-7, Glucose, biological studies 52-53-9, Verapamil 57-11-4, Stearic acid, biological studies 57-11-4D, Stearic **acid, salts** 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 59-23-4, Galactose, biological studies 60-87-7, Promethazine 63-42-3, Lactose 68-04-2, Sodium citrate 69-65-8, Mannitol 72-69-5, Nortriptyline 79-10-7D, Acrylic acid, polymers 79-41-4D, MethAcrylic acid, polymers 127-09-3, Sodium acetate 151-21-3, Sodium lauryl sulfate, biological studies 315-30-0, Allopurinol 469-62-5, Propoxyphene 525-66-6, Propranolol 554-13-2, Lithium carbonate 557-04-0 564-25-0, Doxycycline 657-24-9, Metformin 1343-98-2, Silicic acid 1668-19-5, Doxepin 3458-28-4, Mannose 4070-80-8, Sodium stearyl fumarate 7447-40-7, Potassium chloride (KCl), biological studies 7647-14-5, Sodium chloride, biological studies 7647-15-6, Sodium bromide, biological studies 7757-93-9, Dicalcium phosphate 7778-80-5, Sulfuric acid dipotassium **salt**, biological studies 9000-01-5, Acacia gum 9003-39-8, Polyvinylpyrrolidone 9003-39-8D, Polyvinylpyrrolidone, crosslinked derivs. 9004-34-6D, Cellulose, ethers 9004-35-7, Cellulose acetate 9004-54-0, Dextran, biological studies 9004-57-3, Ethyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9057-02-7, Pullulan 16051-77-7, Isosorbide mononitrate 16068-46-5, Potassium phosphate 22204-53-1, Naproxen 25322-68-3, Polyethylene glycol 26787-78-0, Amoxicillin 27203-92-5, Tramadol 29122-68-7, Atenolol 34911-55-2, Bupropion 42399-41-7, Diltiazem 51384-51-1, Metoprolol 51481-61-9, Cimetidine 59277-89-3, Acyclovir **60142-96-3**, **Gabapentin** 62571-86-2, Captopril

6357-35-5, Ranitidine 66376-36-1, Alendronate 71620-89-8, Reboxetine
3799-24-0, Fexofenadine 83905-01-5, Azithromycin 85441-61-8,
uinapril 85721-33-1, Ciprofloxacin 92665-29-7, Cefprozil
3413-69-5, Venlafaxine 93957-54-1, Fluvastatin 98048-97-6, Fosinopril
00986-85-4, Levofloxacin 103628-46-2, Sumatriptan 104632-26-0,
ramipexole 114798-26-4, Losartan 124832-26-4, Valacyclovir
39755-83-2, Sildenafil 146798-66-5 156907-84-5 179386-43-7,
umanirole
L: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zero-order sustained-release dosage forms)

IT **60142-96-3, Gabapentin**
L: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zero-order sustained-release dosage forms)

RN 60142-96-3 CAPLUS
CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:608551 CAPLUS
DOCUMENT NUMBER: 133:213151
TITLE: Pharmaceutical compositions and methods for improved delivery of hydrophobic therapeutic agents
INVENTOR(S): Patel, Manesh V.; Chen, Feng-Jing
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050007	A1	20000831	WO 2000-US165	20000105
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6294192	B1	20010925	US 1999-258654	19990226
AU 2000022242	A5	20000914	AU 2000-22242	20000105
NZ 771659	B2	20040401		
EP 1158959	A1	20011205	EP 2000-901394	20000105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537317	T2	20021105	JP 2000-600619	20000105

NZ 513810 A 20040227 NZ 2000-513810 20000105
PRIORITY APPLN. INFO.: US 1999-258654 A 19990226
WO 2000-US165 W 20000105

AB The present invention relates to tri...eride-free pharmaceutical compns. for delivery of hydrophobic therape...agents. Compns. of the present invention include a hydrophobic the...tic agent and a carrier, where the carrier is formed from a combination ... a hydrophilic surfactant and a hydrophobic surfactant. Upon dilut...ith an aqueous solvent, the composition forms
a clear, aqueous dispersion of the ...ctants containing the therapeutic agent.
The invention also provides methods ... reatment with hydrophobic therapeutic agents using these compns. A pharmaceutical composition contained cyclosporin 0.14, Cremophor RH-40 0.4..., Arlacel186 0.29, sodium taurocholate 0.26, and propylene gl...ol 0.46 mg.

IC ICM A61K009-127
ICS A61K009-107; A61K038-13

CC 63-6 (Pharmaceuticals)

IT Alcohols, biological studies
Amides, biological studies
Bile acids
Corticosteroids, biological studies
Diglycerides
Esters, biological studies
Fatty acids, biological studies
Glycerides, biological studies
Lecithins
Lysophosphatidic acids
Lysophosphatidylcholines
Lysophosphatidylethanolamines
Lysophosphatidylserines
Lysophospholipids
Monoglycerides
Peptides, biological studies
Phosphatidic acids
Phosphatidylcholines, biological studies
Phosphatidylethanolamines, biological studies
Phosphatidylglycerols
Phosphatidylserines
Phospholipids, biological studies
Polyoxyalkylenes, biological studies
Salts, biological studies
Sex hormones
Sterols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. and methods for improved delivery of hydrophobic therapeutic agents)

IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**salts**; pharmaceutical compns. and methods for improved delivery of hydrophobic therapeu...agents)

IT 50-14-6, Ergocalciferol 50-21-5D, Lactic acid, glycerides 50-24-8, Prednisolone 50-28-2, EStradiol, ...gical studies 50-70-4, Sorbitol, biological studies 51-48-9, L-Thy...ine, biological studies 52-01-7, Spironolactone 55-98-1, Busulphan ...-81-5, 1,2,3-Propanetriol, biological studies 56-81-5D, Glyce... polyethylene fatty acid esters 57-10-3, Hexadecanoic acid, biologica...studies 57-11-4, Octadecanoic acid, biological studies 57-55-6, ...Propanediol, biological studies 57-55-6D, Propylene glycol, ethers ...-33-0, Progesterone, biological studies 57-88-5, Cholesterol, bio...al studies 57-88-5D,

Cholesterol, polyoxyethylene derivs. 60-33-3, 9,12-Octadecadienoic acid (9Z,12Z)-, biological studies 64-17-5, Ethanol, biological studies 66-76-2, Dicoumarol 67-20-9, Nitrofurantoin 67-45-8, Furazolidone 67-63-0, Isopropanol, biological studies 67-96-9, Dihydrotachysterol 67-97-0, Cholecalciferol 69-65-8, Mannitol 71-36-3, Butanol, biological studies 76-57-3, Codeine 76-99-3, Methadone 77-89-4, Acetyl triethylcitrate 77-90-7, Acetyl tributyl citrate 77-92-9D, Citric acid, diglycerides 77-93-0, Triethylcitrate 77-94-1, Tributylcitrate 81-24-3 81-25-4 83-44-3 87-33-2, Isosorbide dinitrate 87-69-4D, Tartaric acid, glycerides, biological studies 90-82-4, Pseudoephedrine 100-51-6, Benzenemethanol, biological studies 102-76-1, Triacetin 104-31-4, Benzonatate 105-37-3, EThyl propionate 105-54-4, Ethyl butyrate 105-60-2, biological studies 105-60-2D, Caprolactam, N-Alkyl derivs. 106-32-1, Ethyl caprylate 107-21-1, 1,2-Ethanediol, biological studies 110-27-0, Isopropyl myristate 111-03-5, Glyceryl monooleate 111-62-6, Crodamol EO 111-90-0, Transcutol 112-80-1, 9-Octadecenoic acid (9Z)-, biological studies 113-15-5, Ergotamine 113-92-8, Chlorpheniramine 115-77-5, biological studies 115-83-3, Pentaerythrityl Tetra stearate 124-07-2, Octanoic acid, biological studies 125-84-8, Aminoglutethimide 126-07-8, Griseofulvin 127-19-5, Dimethylacetamide 128-13-2 141-22-0 142-18-7, Glyceryl monolaurate 142-62-1, Hexanoic acid, biological studies 142-91-6, Isopropyl palmitate 143-07-7, Dodecanoic acid, biological studies 151-41-7, Lauryl sulfate 155-97-5, Pyridostigmine 298-46-4, 5H-Dibenz[b,f]azepine-5-carboxamide 298-57-7, Cinnarizine 298-81-7, Methoxsalen 300-62-9, Amphetamine 302-79-4, Tretinoin 303-49-1, Clomipramine 321-64-2, Tacrine 334-48-5, Decanoic acid 359-83-1, Pentazocine 360-65-6 378-44-9, Betamethasone 404-86-4, Capsaicin 437-38-7, Fentanyl 443-48-1, Metronidazole 463-40-1 474-25-9 475-31-0 511-12-6, Dihydroergotamine 516-35-8 516-50-7 520-85-4, Medroxyprogesterone 542-28-9, δ-Valerolactone 544-35-4, Ethyl linoleate 544-63-8, Tetradecanoic acid, biological studies 577-11-7, Sodium docusate 595-33-5 616-45-5, Pyrrolidone 616-45-5D, Pyrrolidone, N-Alkyl derivs. 623-84-7, Propylene glycol diacetate 640-79-9 675-20-7, 2-Piperidone 872-50-4, N-Methylpyrrolidone, biological studies 1134-47-0, Baclofen 1331-12-0, Propylene glycol monoacetate 1335-71-3, Propylene glycol oleate 1338-39-2, Arlacel 20 1338-43-8, Span 80 1397-89-3, Amphotericin B 1406-16-2, Vitamin D 1406-18-4, Vitamin E 1951-25-3, Amiodarone 1972-08-3, Tetrahydrocannabinol 2687-91-4, N-Ethylpyrrolidone 2687-94-7 2687-96-9 3068-88-0, β-Butyrolactone 3445-11-2 4419-39-0, BeclomethAsone 4759-48-2, Isotretinoin 5104-49-4, Flurbiprofen 5306-85-4, Dimethyl isosorbide 7261-97-4, Dantrolene 7488-99-5, α Carotene 7664-93-9D, Sulfuric **acid**, **salts** alkyl derivs., biological studies 7689-03-4, Camptothecin 8007-43-0, Sorbitan sesquioleate 9002-89-5, Polyvinylalcohol 9002-92-0, Brij 30 9002-96-4 9003-39-8, Polyvinylpyrrolidone 9004-65-3, Hydroxypropyl methylcellulose 9004-74-4, Methoxy polyethylene glycol 9004-81-3, Polyoxyethylene laurate 9004-95-9, Polyoxyethylene cetyl ether 9004-96-0, PEG-32 oleate 9004-98-2, Polyoxyethylene oleyl ether 9004-99-3, Polyoxyethylene stearate 9005-00-9, Polyoxyethylene stearyl ether 9005-02-1, Polyoxyethylene dilaurate 9005-07-6, Polyoxyethylene dioleate 9005-08-7, Polyoxyethylene distearate 9005-32-7D, Alginic **acid**, **salts** 9005-37-2, Propylene glycol alginate 9005-63-4D, Polyoxyethylene sorbitan, derivs. 9005-63-4D, Polyoxyethylene sorbitan, fatty acid esters 9005-64-5, Tween 20 9005-65-6, Polysorbate 80 9005-66-7, Tween 40 9005-67-8, Tween 60 9007-48-1, PLUROLOLEIQUECC497 9011-21-6, Polyoxyethylene glyceryl stearate 9016-45-9 9036-19-5 10238-21-8, Glyburide 10540-29-1, Tamoxifen 11103-57-4, Vitamin A 11140-04-8, Imwitor 988 12001-79-5,

Vitamin K 12619-70-4, Cyclodextrin 12619-70-4D, Cyclodextrin, derivs. 12619-70-4D, Cyclodextrin, hydroxypropyl ethers 13081-97-5, Pentaerythrityl di stearate 14440-80-3, Stearoyl-2-lactylate 14605-22-2 15307-86-5, Diclofenac 15574-96-6, Pizotifen 15686-51-8, Clemastine 15687-27-1, Ibuprofen 18559-94-9, Albuterol 19356-17-3, Calcifediol 20594-83-6, Nalbuphine 20830-75-5, Digoxin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22882-95-7, Isopropyl linoleate 22916-47-8, Miconazole 23288-49-5, Probucol 25168-73-4, Sucrose monostearate 25265-75-2, Butanediol 25322-68-3 25322-69-4, Polypropylene glycol 25339-99-5, Sucrose monolaurate 25523-97-1, Dexchlorpheniramine 25618-55-7D, Polyglycerol, fatty acid esters 25637-84-7, Glyceryl dioleate 25637-97-2, Sucrose dipalmitate 25812-30-0, Gemfibrozil 26266-57-9, Sorbitan monopalmitate 26266-58-0, Sorbitan Trioleate 26402-22-2, Glyceryl monocaprate 26402-26-6, Glyceryl monocaprylate 26446-38-8, Sucrose monopalmitate 27154-43-4D, Piperidone, N-Alkyl derivs. 27195-16-0, Sucrose distearate 27203-92-5, TRamadol 27638-00-2, Glyceryl dilaurate 29094-61-9, Glipizide 29767-20-2, Teniposide 31692-85-0, Glycofurol 32222-06-3, Calcitriol 33069-62-4, Paclitaxel 33419-42-0, Etoposide 34911-55-2, Bupropion 36354-80-0, Glyceryl dicaprylate 37321-62-3, Lauroglycol 38304-91-5, Minoxidil 41340-25-4, Etodolac 42924-53-8, Nabumetone 43200-80-2, Zopiclone 49562-28-9, Fenofibrate 49697-38-3, Rimexolone 51333-22-3, Budesonide 51481-61-9, Cimetidine 51938-44-4, Sorbitan sesquistearate 52581-71-2, Volpo 3 53123-88-9, Sirolimus 53168-42-6, Myvacet 9-45 53179-11-6, Loperamide 53230-10-7, Mefloquine 53988-07-1, Glyceryl dicaprate 54392-26-6, Sorbitan monoisostearate 54965-21-8, Albendazole 55079-83-9, Acitretin 55142-85-3, Ticlopidine 57107-97-8, Polyoxyethylene glyceryl oleate 59467-70-8, Midazolam 59865-13-3, Cyclosporine **60142-96-3**, **Gabapentin** 61379-65-5, Rifapentine 61869-08-7 62013-04-1, Dirithromycin 62356-64-3 63590-64-7, Terazosin 63612-50-0, Nilutamide 63675-72-9, Nisoldipine 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 68506-86-5, Vigabatrin

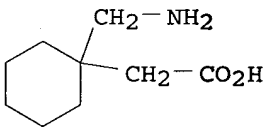
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. and methods for improved delivery of hydrophobic therapeutic agents)

IT **60142-96-3, Gabapentin**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. and methods for improved delivery of hydrophobic therapeutic agents)

RN 60142-96-3 CAPLUS

CN Cyclohexaneacetic acid, 1-(aminomethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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    Derwent Chemistry Resource display fields  <<<

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                ACID (3A) AMINOMETHYL
L2        50035 SEA FILE=WPIDS ABB=ON  PLU=ON  TARTARIC OR TARTARATE OR MALEIC
                OR MALEATE OR ETHANEDISULFONIC  OR ETHANEDISULPHONIC OR ETHANE
                (W) (DISULFONIC OR DISULPHONIC)
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L5           80 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (S) SALT#
L6            3 SEA FILE=WPIDS ABB=ON  PLU=ON  L2 AND L5
L7           44 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (5A) SALT#
L8           39 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (3A) SALT#
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                ACID (3A) AMINOMETHYL
L2        50035 SEA FILE=WPIDS ABB=ON  PLU=ON  TARTARIC OR TARTARATE OR MALEIC
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L5           80 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (S) SALT#
L6            3 SEA FILE=WPIDS ABB=ON  PLU=ON  L2 AND L5
L7           44 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (5A) SALT#
L8           39 SEA FILE=WPIDS ABB=ON  PLU=ON  L1 (3A) SALT#
L9           80 SEA FILE=WPIDS ABB=ON  PLU=ON  L5 OR L7 OR L8
L10           4 SEA FILE=WPIDS ABB=ON  PLU=ON  L9 AND CRYS?
L11          11 SEA FILE=WPIDS ABB=ON  PLU=ON  L4 OR L6 OR L10
```

L12 7 SEA FILE=WPIDS ABB=ON PLU=ON L3 NOT L11

=> d .wp l11 -11 ; d .wp l12 1-7

L11 ANSWER 1 OF 11 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2004-652083 [63] WPIDS
DNC C2004-233326
TI Preparation of **gabapentin** in **crystalline** form II useful for treating cerebral disorders involves dissolving **gabapentin** hydrochloride in dry ethanol; filtering insoluble **salts**; adding tertiary amine; cooling and seeding.
DC B05
IN ASSANELLI, C; BREVIGLIERI, G; CONTRINI, S
PA (ASSA-I) ASSANELLI C; (BREV-I) BREVIGLIERI G; (CONT-I) CONTRINI S
CYC 1
PI US 2004176639 A1 20040909 (200463)* 3
ADT US 2004176639 A1 US 2004-769886 20040203
PRAI IT 2003-MI176 20030204
AB US2004176639 A UPAB: 20041001
NOVELTY - Preparation of pure **gabapentin** in **crystalline** form II (I) involves dissolving **gabapentin** hydrochloride in dry ethanol; filtering or centrifuging off insoluble inorganic **salts**; adding tertiary amine and water to the ethanol solution free from inorganic **salts**; cooling to 10 - 20 deg. C; seeding with **gabapentin** form II; further cooling to 5 - -5 deg. C; and recovering precipitated (I).
ACTIVITY - Cerebroprotective.
MECHANISM OF ACTION - None given.
USE - For preparation of pure gabapentin in **crystalline** form II (claimed) useful for treating cerebral disorders.
ADVANTAGE - The process can be carried out in a simple manner, with notable saving of time, apparatus and labor. The process is easy and provides (I) in higher yield without recovering **gabapentin** hydrochloride free of **salts** and without producing **gabapentin** form III.
Dwg.0/0
TECH UPTX: 20041001
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Process: The solution added with the tertiary amine and water is cooled to 15 degreesC, seeded with **gabapentin** form II and after 4 - 8 hours is further cooled to about 0 degreesC. The resulting **gabapentin** form II is further purified by suspension in ethanol (approximately 10 vol.%) containing water (about 10 vol.%); heating for about 10 - 15 minutes at 35 - 45 degreesC; and standing overnight at room temperature.
Preferred Components: The wt./vol. ratio of **gabapentin** hydrochloride to dry ethanol is 1:6 - 1:9 (preferably 1:6.5 - 1:8). The tertiary amine is added in an amount of 1 - 1.25 (preferably 1.1 -1.2) mol/mol of hydrochloride. The amount of water added to the ethanol solution free from inorganic **salts** is 7 - 10 (preferably 8 - 9) vol.%. The triethylamine is N-ethyl-diisopropylamine.

L11 ANSWER 2 OF 11 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2004-375502 [35] WPIDS
CR 2004-399893 [37]
DNC C2004-141139
TI Preparation of gabapentin tablet involves forming mixture by dry mixing of first portion of binder with gabapentin and/or excipient, followed by addition of second portion of binder.
DC A96 B05

IN GOGIA, A; MALIK, R; MANIKANDAN, R; ROY, S B
PA (RANB-N) RANBAXY LAB LTD
CYC 106
PI WO 2004032905 A1 20040422 (200435)* EN 18
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP
KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG
PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ
VC VN YU ZA ZM ZW
AU 2003267732 A1 20040504 (200465)
ADT WO 2004032905 A1 WO 2003-IB4436 20031008; AU 2003267732 A1 AU 2003-267732 20031008
FDT AU 2003267732 A1 Based on WO 2004032905
PRAI IN 2002-DE1023 20021008
AB WO2004032905 A UPAB: 20041011
NOVELTY - Preparation of a stable gabapentin tablet involves forming a mixture by dry mixing of a first portion of a binder with the gabapentin and/or at least one excipient, followed by the addition of a second portion of the binder. The second portion of the binder is in the form of a solution or dispersion.

ACTIVITY - Anticonvulsant; Neuroprotective; Analgesic; Antimigraine.

MECHANISM OF ACTION - None given.

USE - For treating epilepsy, neuropathic pain, post poliomyelitis pain, amyotrophic lateral sclerosis, pain of diabetic neuropathy; providing anticonvulsant therapy; controlling rapid cycling and mixed bipolar state; and as a prophylactic agent for patients with migraine headache (all claimed).

ADVANTAGE - The tablets are not only free from capping and lamination defects but also has better hardness and is stable. The addition of binder in two portions requires minimum use of solvent, which makes it possible to add the binder solution in single step, improves safety and environmental impact of the process, and reduces the duration of exposure of gabapentin which further reduces the likelihood of polymorph conversion and/or change in **crystal** structure in gabapentin.

Dwg.0/0

TECH UPTX: 20040603

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: The method further involves mixing the second portion of the binder with the mixture to form granules; drying the granules; mixing at least one excipient with the granules; and then compressing into tablets, followed by coating the tablet. The binder solution or dispersion is prepared in water alone or in a mixture of water with at least one of ethanol, isopropyl alcohol or acetone (preferably in the mixture of water and ethanol).

Preferred Component: The ratio of drug to binder is 1:0.01 - 1:1. The binder is at least one hydroxypropyl cellulose, hydroxypropyl methylcellulose, polyvinylpyrrolidone, copolyvidone or sugar (preferably hydroxypropyl cellulose or copolyvidone). The **gabapentin** comprises the free base hydrated form, monohydrate or its **salt.** The **gabapentin** has an anion of the mineral acid at most 100 (preferably 20 - 100) ppm as calculated by chloride content. The excipient is disintegrant (0.5 - 15 wt./wt.%) (preferably microcrystalline cellulose, sodium starch glycolate, crosslinked carboxy methylcellulose or crospovidone, especially crospovidone), filler (preferably lactose, microcrystalline cellulose, mannitol or dicalcium phosphate), stabilizer (0.1 - 10 wt./wt.%) (preferably poloxamer, cremophor, anionic surfactant, cationic surfactant or nonionic surfactant), lubricant (preferably magnesium stearate, steric acid or stearyl fumarate), colorant, flavor or glidant. The coating comprises at least one hydrophilic polymer,

hydroxypropyl cellulose, hydroxypropyl methylcellulose, polyvinylpyrrolidone or polyvinyl alcohol.
Preferred Tablet: The tablet has a lactam content less than 0.1, less than 0.2 and less than 0.4 wt.% of **gabapentin** after 1, 2 and 3 months respectively of storage at 40 degrees C and 75% humidity. The coated tablet has a friability of less than 1 (preferably 0.1) wt./wt.%. The uncoated tablet has a hardness of 10 - 30 (preferably 20 - 25) Kp.

L11 ANSWER 3 OF 11 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2004-081967 [08] WPIDS
DNC C2004-033732
TI Sustained release tablet useful for treating epilepsy comprises gabapentin and at least one rate-controlling polymer.
DC A11 A14 A25 A96 B05 B07
IN CHAWLA, M; RAGHUVANSHI, R S; RAMPAL, A
PA (RANB-N) RANBAXY LAB LTD
CYC 103
PI WO 2003103634 A1 20031218 (200408)* EN 29
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL
PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU
ZA ZM ZW
AU 2003232398 A1 20031222 (200445)
ADT WO 2003103634 A1 WO 2003-IB2166 20030606; AU 2003232398 A1 AU 2003-232398 20030606
FDT AU 2003232398 A1 Based on WO 2003103634
PRAI IN 2002-DE616 20020607
AB WO2003103634 A UPAB: 20040202
NOVELTY - A sustained release tablet comprises **gabapentin** (a) or its **salts** or hydrates; and at least one rate-controlling polymer (b). The tablet provides plasma levels of **gabapentin** for up to 12 hours.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the preparation of the tablet involving granulating a mixture of (a) and (b) with water and/or a binder solution followed by compressing the granules into a tablet.
ACTIVITY - Anticonvulsant.
MECHANISM OF ACTION - None given.
USE - For treating medical conditions e.g. epilepsy (claimed).
ADVANTAGE - The tablet releases at most approx. 50% of the drug in 1 hour, at most approx. 65% of the drug in 2 hours, and at most approx. 85% of the drug in 4 hours, when measured in a USP type II dissolution apparatus at 50 rpm, at 37 plus or minus 0.5 deg. C in 0.06 N hydrochloric acid (900 ml).The tablet when administered twice per day provides comparable bioavailability with respect to a tablet or capsule containing gabapentin administered three times per day under fasting conditions for similar cumulative daily dose.
Dwg.0/0
TECH UPTX: 20040202
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Tablet: The tablet comprises (b) (5 - 80 (preferably 5 - 70, especially 5 - 60) wt.%). The tablet further comprises at least one excipient (preferably diluent, lubricant, glidant, binder, or stabilizer). The tablet is configured to release gabapentin in the stomach by diffusion or erosion.

TECHNOLOGY FOCUS - POLYMERS - Preferred Polymers: (b) is at least one of polyvinylpyrrolidone, cellulosic polymer, vinylacetate copolymer,

alginate, xanthan gum, guar gum, starch and starch based polymer, polyethylene oxide, methacrylic acid copolymer, **maleic** anhydride/methyl vinyl ether copolymer or derivatives, ethyl cellulose, cellulose acetate, methacrylate, acrylic acid polymer and high copolymer, high molecular weight polyvinyl alcohol, or wax (preferably cellulosic polymer, especially hydroxypropyl methylcellulose, hydroxypropylcellulose, hydroxyethylcellulose, or methylcellulose, particularly hydroxypropyl methylcellulose of viscosity 100 - 100000 (preferably 4000 - 15000) cps , hydroxypropylcellulose of viscosity 7 - 30000 (preferably 4000 - 15000) cps, hydroxyethylcellulose). (b) swells to form a polymeric matrix after contact with fluid having properties of gastric fluids. The diluent is microcrystalline cellulose or dry starch. The binder is polyvinylpyrrolidone, polyvinylpyrrolidone/vinylacetate copolymer, xanthan gum, guar gum, cellulose gum, carboxymethylcellulose, methylcellulose, hydroxypropyl methylcellulose, hydroxypropyl cellulose, gelatin, starch, or pregelatinized starch. The stabilizer comprises polyoxamer.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: The diluent is powdered sugar, lactose, mannitol, or sorbitol. The lubricant is stearic acid, vegetable oil, calcium stearate, zinc stearate, or magnesium stearate.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Components: The diluent is calcium phosphate, calcium sulfate, or kaolin. The lubricant is talc. The glidant is talc or silicon dioxide.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Component: The glidant is cornstarch.

L11 ANSWER 4 OF 11 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2003-645897 [61] WPIDS
CR 2003-645899 [61]
DNC C2003-176613
TI Solid dosage useful for sustained release of active agent comprises matrix core containing ethyl cellulose and a water-soluble active agent, and hydrophobic polymer coating encasing the entire matrix core.
DC A96 B05 B07
IN COX, S R; GANORKAR, L D; HEIMLICH, J M; LEE, E J; NOACK, R M; VERHAGE, R R; JOHN, L E
PA (COXS-I) COX S R; (GANO-I) GANORKAR L D; (HEIM-I) HEIMLICH J M; (LEEE-I) LEE E J; (NOAC-I) NOACK R M; (VERH-I) VERHAGE R R; (PHAA) PHARMACIA CORP
CYC 103
PI WO 2003053402 A1 20030703 (200361)* EN 17
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
US 2003129236 A1 20030710 (200361)
US 2003133982 A1 20030717 (200361)
AU 2002358270 A1 20030709 (200428)
EP 1455751 A1 20040915 (200460) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
ADT WO 2003053402 A1 WO 2002-US41104 20021219; US 2003129236 A1 Provisional US 2001-342642P 20011220, US 2002-324718 20021219; US 2003133982 A1 Provisional US 2001-342642P 20011220, Provisional US 2001-342819P 20011220, US 2002-324719 20021219; AU 2002358270 A1 AU 2002-358270

20021219; EP 1455751 A1 EP 2002-792508 20021219, WO 2002-US41104 20021219
FDT AU 2002358270 A1 Based on WO 2003053402; EP 1455751 A1 Based on WO 2003053402
PRAI US 2001-342819P 20011220; US 2001-342642P 20011220; US 2002-324718 20021219; US 2002-324719 20021219
AB WO2003053402 A UPAB: 20040920
NOVELTY - Solid dosage comprises matrix core containing intragranular ethyl cellulose and a water-soluble active agent granulated and compressed together with extragranular ethylcellulose, and film coating containing hydrophobic polymer. The film coating encases the entire matrix core.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for preparation of the solid dosage form involving:

(a) preparing a first mixture containing the active agent and intragranular ethylcellulose;

(b) granulating the first mixture to obtain a granular product;

(c) preparing a second mixture containing extragranular ethylcellulose;

(d) preparing a third mixture comprising the granular product and the second mixture;

(e) compressing the third mixture to form the matrix core; and

(f) applying the film coating to the matrix core.

USE - As a solid dosage form (claimed) for sustained release of active agent in the form of highly soluble drugs that require a high drug load.

ADVANTAGE - The solid dosage form provides release of the active agent at a zero order rate for at least 8 (preferably at least 12) hours after oral administration. The preparation of solid dosage form is simple and allows manufacture of the tablets on a production scale. The preparation does not involve use solvent or heat. The solid dosage has dual advantage in allowing ease of manufacture and affording medicament release in a substantially linear fashion over an extended period of time. Dwg.0/3

TECH UPTX: 20030923
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Agent: The active agent is reboxetine, clindamycin, (-)-S-3-(3-methylsulfonylphenyl)-N-n-propylpiperidine, sumanirole, pramipexole, atenolol, propoxyphene, metformin, metoprolol, amitriptyline, ranitidine, fexofenadine, quinapril, sildenafil, tramadol, verapamil, **gabapentin**, potassium chloride, alendronate, bupropion, levofloxacin, doxycycline, venlafaxine, allopurinol, isosorbide mononitrate, fosonipril, propanolol, promethazine, captopril fluvastatin, cimetidine, sumatriptan, nortriptyline, naproxen, calacyclovir, doxepin, amoxicillin, azithromycin, diltiazem, cefprozil, acyclovir, ciprofloxacin, losartan or their **salts** (preferably reboxetine, clindamycin, (-)-S-3-(3-methylsulfonylphenyl)-N-n-propylpiperidine hydrochloride, sumanirole, pramipexole or their **salts**, especially clindamycin HCl or clindamycin crystalline free base, particularly clindamycin HCl). The active agent is present in an amount of 1-85 wt.% of the matrix core. Preferred Components: The intragranular and extragranular ethylcellulose together are present in an amount of 15 - 99 wt.% of the matrix core. The matrix core further comprises a filter (up to 50 wt.%) and a lubricant (0.1-3 wt.%). The amount of film coating is 1-33, preferably 3-15 wt.% relative to the weight of the matrix core. The film coating further comprises a pore former (up to 50 wt.%). The matrix core comprises: ethyl cellulose (20-45 wt.%), microcrystalline cellulose (up to 50 wt.%) and the water soluble active agent (40-80 wt.%). The film forming coating comprises ethyl cellulose (50-95 wt.%) and hydroxypropyl methyl cellulose (5-50 wt.%).

TECHNOLOGY FOCUS - POLYMERS - Preferred Filler: The filler is

microcrystalline cellulose, starches, gelatin or polyvinylpyrrolidinone (preferably microcrystalline cellulose). The hydrophobic polymer is wax, wax-like substance, fatty alcohol, shellac, zein, hydrogenated vegetable oil, water insoluble cellulose, cellulose acetate, polymers of acrylic acid or polymers of methacrylic acid (preferably ethyl cellulose). The pore former is hydroxypropyl methyl cellulose, cellulose ether polyvinylpyrrolidone, cross-linked polyvinylpyrrolidone, polyethylene oxide, polyethylene glycol or pullulan (preferably hydroxypropyl methyl cellulose). The lubricant is solid polyethylene glycol.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Filler: The filler is sodium citrate, dicalcium phosphate, colloidal silicon dioxide, silicic acid or alginate. The pore former is lithium carbonate, sodium chloride, sodium bromide, potassium chloride, potassium sulfate, potassium phosphate, sodium acetate or sodium citrate.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Filler: The filler is lactose, sucrose, glucose, mannitol or acacia. The lubricant is stearic acid salt, stearic acid, stearate family, sodium stearyl fumarate or sodium lauryl sulfate (preferably magnesium stearate). The pore former is protein-derived material, dextran, sucrose, glucose, fructose, mannitol, lactose, mannose, galactose or sorbitol.

L11 ANSWER 5 OF 11 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2003-449229 [42] WPIDS
DNC C2003-119234
TI Sustained release gastric retentive dosage form useful for restricted delivery of an active agent in the lower gastrointestinal tract comprises the agent incorporated in a matrix of a polymer.
DC B05
IN BERNER, B; LOUIE-HELM, J
PA (DEPO-N) DEPOMED INC; (BERN-I) BERNER B; (LOUI-I) LOUIE-HELM J
CYC 101
PI WO 2003035041 A1 20030501 (200342)* EN 31
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
CA 2409552 A1 20030425 (200342) EN
US 2003104052 A1 20030605 (200344)
EP 1439826 A1 20040728 (200449) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
AU 2002349934 A1 20030506 (200460)
US 2004185105 A1 20040923 (200463)
ADT WO 2003035041 A1 WO 2002-US34297 20021025; CA 2409552 A1 CA 2002-2409552 20021023; US 2003104052 A1 CIP of US 2001-45816 20011025, US 2001-24932 20011218; EP 1439826 A1 EP 2002-786524 20021025, WO 2002-US34297 20021025; AU 2002349934 A1 AU 2002-349934 20021025; US 2004185105 A1 CIP of US 2001-45816 20011025, Div ex US 2001-24932 20011218, US 2004-769574 20040129
FDT EP 1439826 A1 Based on WO 2003035041; AU 2002349934 A1 Based on WO 2003035041
PRAI US 2001-24932 20011218; US 2001-45816 20011025; US 2004-769574 20040129
AB WO2003035041 A UPAB: 20030703
NOVELTY - Dosage form (D1) comprises an active agent incorporated in a matrix of at least one polymer (I). (I) Swells in presence of water in

gastric fluid providing gastric retention during the fed mode, and erodes gradually within the gastrointestinal tract releasing the active agent throughout a determinable period.

DETAILED DESCRIPTION - Dosage form (D1) comprises an active agent incorporated in a matrix of at least one polymer (I). (I) Swells in presence of water in gastric fluid providing gastric retention during the fed mode, and erodes gradually within the gastrointestinal tract releasing the active agent throughout a determinable period. The ratio of the erosion rate (ER) obtained in vitro for (D1) using USP disintegration test equipment to the dissolution rate (DR) obtained in vitro for (D1) using USP dissolution test equipment is 1.2:1-5:1 (preferably 1.5:1-2:1).

INDEPENDENT CLAIMS are also included for:

(1) treatment of a bacterial infection responsive to the oral administration of ciprofloxacin in human involving administering (D1) containing ciprofloxacin or its acid addition salt; and

(2) selection of controlled release dosage form involving preparing several candidate dosage forms (D2), obtaining ER and DR in vitro for each (D2), and selecting (D2) having the ER to DR ratio of 1.2:1-3:1. Each of (D2) comprises a polymer (II) and an active agent incorporated into it. The selected (D2) will have a predetermined drug release profile in vivo.

ACTIVITY - Antibacterial.

MECHANISM OF ACTION - None given.

USE - For sustained delivery of the pharmacological agent to the stomach, duodenum and upper small intestine with restricted delivery to the lower intestinal tract and colon; for treating infection with Mycobacterium avium complex, Pseudomonas, Shigella, Salmonella, toxigenic Escherichia coli, Campylobacter, Enterobacter and Bacillus anthracis. For selecting (D2) which is useful for controlled release of active agent (claimed).

ADVANTAGE - (D1) Gives sustained release of the agent to the stomach, duodenum and upper small intestine but restricted delivery to the lower intestinal tract and colon. (D1) Is an erodible, gastric retentive oral drug dosage form that delays the passage of the agent, improves bioavailability of the agent, avoids the need for large dosage, reduces the number of daily doses and lowers the side effects. The gastric retentive dosage form facilitates the delivery of broad range of drugs including water-soluble and sparingly soluble drugs by gradual erosion. The polymer swells in the presence of water in gastric fluid to an increased size facilitating retention of active agent in the upper gastrointestinal (GI) tract of an individual in the fed mode. The gastric retentive dosage forms minimize and eliminate problems (e.g. the overgrowth of detrimental intestinal flora resulting from drugs that are toxic to the normal intestinal flora by delivering the bulk drug dose to the upper gastrointestinal tract (GI)) and restricting little or no drug to reach the lower GI). The dosage forms can also prevent chemical degradation of drugs by intestinal enzymes, loss of bioavailability of the drug due to its leaving the acidic environment of the stomach, and chemical degradation of the drug in the neutral to alkaline environment of GI tract in presence of the polymer matrix.

Dwg.0/9

TECH UPTX: 20030703

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: Dosage form(D1) contains 0.01-80 (preferably 60-80) vol.% of active agent. At least 90 wt.% of (D1) disintegrates in vitro in 1 .5-12 (preferably 1.5-9) hours using USP disintegration test equipment and at least 90% of (a1) is released in vitro in less than 25 (preferably 20, especially less than 16) hours using USP dissolution test equipment. (D1) is comprised of a tablet or a capsule.

Preferred Agent: The aqueous solubility of active agent decreases with increasing pH, hence the active agent is slightly soluble to soluble in

water at a pH of 1-4 (preferably 1-2) but becomes insoluble at pH above 5 (preferably 5-8, especially 5-7.5). The active agent is an antibiotic selected from ciprofloxacin, minocycline, their acid addition **salts** (preferably ciprofloxacin hydrochloride or minocycline hydrochloride), furosemide, **gabapentin**, losartan, budesonide, or a Heliobacter pylori eradicant, preferably is bismuth subsalicylate, bismuth citrate, amoxicillin, tetracycline, minocycline, doxycycline, clarithromycin, thiamphenicol, metronidazole, omeprazole, ranitidine, cimetidine and/or famotidine (preferably bismuth subsalicylate). The active agent contained within a vesicle or enterically coated, is water-soluble but rendered sparingly water-soluble by the vesicle. The vesicle is liposome, proteinoid and amino acid microsphere, nanoparticle (e.g. nanosphere, nanocrystal or nanocapsule), or pharmacosome.

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: (I) Is crosslinked in (D1) and selected from polyalkylene oxide (e.g. poly(ethylene oxide) and/or poly(ethylene oxide-co-propylene oxide)); cellulosic polymer; acrylic acid and methacrylic acid polymer, and their esters; **maleic** anhydride polymer; polymaleic acid; poly(acrylamide); poly(olefinic alcohol); poly(N-vinyl lactam); polyol; polyoxyethylated saccharide; polyoxazoline; polyvinylamine; polyvinylacetate; polyimine; starch and starch-based polymer; polyurethane hydrogel; chitosan; polysaccharide gum; zein; shellac-based polymer and/or copolymer (preferably polyalkylene oxide, cellulosic polymer and/or gum). (I) Has a number average molecular weight of 5000-20000000. (I) And (II) are biocompatible and hydrophilic.

L11 ANSWER 6 OF 11 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2002-154123 [20] WPIDS
CR 1999-131846 [11]; 2001-380692 [40]
DNC C2002-048075
TI Pharmaceutical composition useful for inhibiting a cerebral neurovascular disorder or muscular headache in a human involves intranasally administering at least one local anesthetic.
DC B05
IN LEVIN, B H
PA (LEVI-I) LEVIN B H
CYC 1
PI US 2001055607 A1 20011227 (200220)* 37
US 6432986 B1 20020813 (200255)
ADT US 2001055607 A1 Provisional US 1997-90110P 19970721, Provisional US 1998-72845P 19980128, Provisional US 1998-84559P 19980506, US 1998-118615 19980717; US 6432986 B1 Provisional US 1997-90110P 19970721, Provisional US 1998-72845P 19980128, Provisional US 1998-84559P 19980506, US 1998-118615 19980717
PRAI US 1998-118615 19980717; US 1997-90110P 19970721;
US 1998-72845P 19980128; US 1998-84559P 19980506
AB US2001055607 A UPAB: 20020829
NOVELTY - A pharmaceutical composition formulated for intranasal delivery comprises at least one local anesthetic.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are disclosed for the following:

(1) systemically administering an active agent to a mammal involves non-intravenously administering the composition;

(2) inhibiting a cerebral neurovascular disorder involving anaesthetizing a nerve structure associated with the disorder; and

(3) a kit comprising the composition and an applicator for intranasally administering the composition to patient.

ACTIVITY - Cerebroprotective; vasotropic; antimigraine.

A 25- year - old female patient afflicted with recurring serve

migraine (rating 5-8 on pain scale), and acute migraine episodes associated with nausea and visual changes; and used to experience one acute migraine episode per week and one severe acute migraine episode per month associated with menses was treated dorsonasally with ropivacaine using cotton swab technique. The patient had constantly experienced relief from all the symptoms of her cerebral neurovascular disorder (CNVD) episode within 3 - 5 minutes.

MECHANISM OF ACTION - Neurotransmitter inhibitor; nitric oxide inhibitor.

USE - For inhibiting a cerebral neurovascular disorder (CNVD) such as tinnitus, cerebrovascular spasm, seizure, a disorder manifested during or after and associated with an acute ischemic event, and a neurovascular headache such as migraine, cluster headache and a headache associated with a vascular disease (claimed).

ADVANTAGE - The composition decreases the frequency of recurrence and/or the severity of (CNVD) episodes in the patient. The intranasal administration provides high local concentration of the composition in a relevant neural structure, utilizing lesser amount of drug administered than would be necessary to administer via different route. The effective period of composition at least one (preferably at least two) hours.
Dwg.0/3

TECH UPTX: 20020402

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Kit: The applicator is selected from an anatomically-shaped applicator; a metered dose, non-metered dose, squeezable, pump, spray, foam, powder, an inhalation or an aerosol dispenser; a dispenser containing a propellant, a patch comprising the composition, an implant comprising the composition, a soft pipette with an elastomeric bulb in fluid communication with a reservoir containing the composition, a dropper for directing the composition past the conchae of the patient to a dorsonasal nerve structure, a swab having an absorbent portion impregnated with the composition, a swab having an anatomically-shaped portion comprising an absorbent portion impregnated with the composition, or a swab having a compressed absorbent containing the composition. The kit further comprises instructional material describing about the intranasal administration of the composition to a human.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition - The composition is long acting local anesthetic composition and comprises at least one long-acting local anesthetic (0.01 - 53 wt.%). The composition comprises a eutectic mixture of at least one local anesthetic and a eutectic ingredient, and further comprises a carrier and an active agent. Preferred Components: the long-acting local anesthetic is a long-acting local anesthetic, a persistent local anesthetic or sustained release formulation of a local anesthetic. The long-acting local anesthetic is selected from ambucaine, amalanone, amylocaine, benoxinate, beloxycaine, biphenamine, bupivacaine, levo-bupivacaine, butacaine, butamben, butanilicicaine, butethamine, butoxycaine, carticaine, 2-chloro-procaine, cocaethylene, cocaine, cyclomethycaine, dibucaine, dimethisoquin, dimethocaine, diperodon, dyelonine, ecgonidine, ecgonine, ethyl aminobenzoate, ethyl chloride, levo-etidocaine, etidocaine, dextro-etidocaine, para-eucaine, euprocin, fenalcomine, fomocaine, hexylcaine, hydroxyprocaine, hydroxytetracaine, isobutyl para-aminobenzoate, leucinocaine mesylate, levoxadrol, lidocaine, lidocaine salicylate monohydrate, meperidine, levo-mepivacaine, mepivacaine, meprylcame, metabutoxycaine, methyl chloride, myrtecaine, naepaine, octacaine, orthocaine, oxelhazaiae, parethoxycaiae, phenacaine, phenol, pipecoloxylidide, piperocaine, piridocaine, polidocanol, pramoxine, sameridine, prilocaine, procaine, propanocaine, proparacaine, propipocaine, propoxycaine, pseudococaine, pyrrocaine, quinine urea, risocaine, ropivacaine, levo-ropivacaine, salicyl alcohol, tetracaine,

tolycaine, trimecaine, veratridine, zolamine, 2-alkyl-2-alkylammo-2', 6'-acetoxy-lidide compound, glycerol 1,2-bis-aminoalkyl ether compound, benzisoxazole compound, ortho-aminoalkylsalicylate compound, heterocyclic phenoxyamine compound, 2-substituted imidazo(1,2-A)pyridine compound, 3-aryl substituted imidazo(1,2-A)pyridine compound, polyorganophosphazene compound, tert-alkylamino-lower acyl-xylidide compound, amidinourea compound, 3-(5'-adenylate) of a lincomycin compound, 3-(5'-adenylate) of a clindamycin compound, N-substituted derivative of a 1-(4'-alkylsulfonylphenyl)-2-amino-1,3-propanediol compound, tert-aminoalkoxyphenyl ether compound, adenosine compound; adenosine, adenosine monophosphate, adenosine diphosphate, or adenosine triphosphate; lauryl polyglycol ether compound, 2-(meta-alkylaminoalkyl)-3-(4-substituted-benzylidene)phthalimidine compound, a 2-(omega-dialkylaminoalkyl)-3-(4-substituted-benzylidene)phthalimidine compound, N,N,N-triethyl-N-alkyl ammonium salt, L-N-n-propylpipecolic acid-2,6-xylidide compound, polymer comprising repeating units of at least one local anesthetic moieties, N-substituted 4-piperidinecarboxamide compound, N-substituted 4-phenyl-4-piperidinecarboxamide compound, isopropylmethyl-(2-(4-propoxy-phenoxy)-ethyl)-amine, compound of formula (I) or their derivative (preferably bupivacaine, levo-bupivacaine, ropivacaine, levo-ropivacaine, tetracaine, etidocaine, levo-etidocaine, dextro-etidocaine, levo-ropivacaine, bupivacaine or levo-mepivacainebupivacaine, especially ropivacaine, levo-ropivacaine, bupivacaine or levo-bupivacaine). The carrier is jelly, creme, gel, semi-solid, liquid, droplet, aerosol, powder, microsome, liposome, emulsion, sol-gel, foam, sustained release, degradable polymer, impregnated film, impregnated fiber, impregnated patch, coated film, coated fiber, coated patch, flexible solid, semisolid carrier, polymeric matrix, suspended microspheres, thermoreversibie gel, eutectic mixture, thermoreversible gel or fluid which exhibits an increase in viscosity in a human nasal cavity. The active agent is a vasoconstrictor, epinephrine, norepinephrine, phenylephrine, methysergide, propanolol, a calcium channel blocker, verapamil, ergot, an ergotamine preparation, dihydroergotamine, serotonin agonist, sumatriptan, zolmitriptan, rizatriptan, naratriptan, chroman compound, aspirin, acetaminophen, non-steroidal antiinflammatory drug, caffeine, narcotic, butorphanol tartrate, meperidine, mast cell degranulation inhibitor, cromolyn sodium, eucalyptol, tetrodotoxin, desoxytetrodotoxin, saxitoxin, organic acid, sulfite salt, **acid salt**, glucocorticoid compound, steroid ester, magnesium or lithium ions, centrally-acting analgesic, beta blocker, agent that increases cerebral levels of gamma-aminobutyric acid, butalbital, drug that increases cerebral levels of gamma-aminobutyric acid, benzodiazepine, valproat, **gabapentin**, divalproex sodium, tri-cyclic antidepressant, narcotic analgesic, oral muscle relaxant, tranquilizer or muscle relaxant.
R1 - R4 = as defined in WO9521821.
Preferred Method: The method involves anaesthetizing the nerve structure by performing acupuncture upon the nerve structure, applying an electrical potential to the nerve structure, applying an electromagnetic potential to the nerve structure, followed by administering the composition to the patient.

L11 ANSWER 7 OF 11 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2001-475649 [51] WPIDS
CR 2000-587124 [55]; 2001-091750 [10]; 2001-244222 [25]; 2002-508310 [54]; 2002-556413 [59]; 2003-615989 [58]; 2003-678184 [64]; 2004-141477 [14]; 2004-178820 [17]; 2004-190101 [18]
DNC C2001-142565
TI Solid composition for delivery of active agents e.g. glyburide comprises carrier optionally containing a substrate having an encapsulation coat containing hydrophilic surfactants e.g. polyoxyethylene alkylethers.

DC A96 B05 B07
IN CHEN, F; PATEL, M V
PA (LIPO-N) LIPOCINE INC; (CHEN-I) CHEN F; (PATE-I) PATEL M V
CYC 95
PI WO 2001037808 A1 20010531 (200151)* EN 106
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
US 6248363 B1 20010619 (200151)
AU 2001017981 A 20010604 (200153)
EP 1233756 A1 20020828 (200264) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2003064097 A1 20030403 (200325)
US 6569463 B2 20030527 (200337)
JP 2003517470 W 20030527 (200344) 118
US 2003215496 A1 20031120 (200377)
ADT WO 2001037808 A1 WO 2000-US32255 20001122; US 6248363 B1 US 1999-447690 19991123; AU 2001017981 A AU 2001-17981 20001122; EP 1233756 A1 EP 2000-980761 20001122, WO 2000-US32255 20001122; US 2003064097 A1 Div ex US 1999-447690 19991123, US 2001-800593 20010306; US 6569463 B2 Div ex US 1999-447690 19991123, US 2001-800593 20010306; JP 2003517470 W WO 2000-US32255 20001122, JP 2001-539423 20001122; US 2003215496 A1 Div ex US 1999-447690 19991123, Cont of US 2001-800593 20010306, US 2003-428341 20030501
FDT AU 2001017981 A Based on WO 2001037808; EP 1233756 A1 Based on WO 2001037808; US 2003064097 A1 Div ex US 6248363; US 6569463 B2 Div ex US 6248363; JP 2003517470 W Based on WO 2001037808; US 2003215496 A1 Div ex US 6248363, Cont of US 6569463
PRAI US 1999-447690 19991123; US 2001-800593 20010306; US 2003-428341 20030501
AB WO 200137808 A UPAB: 20040426
NOVELTY - Composition for improved delivery of active agent comprising a solid carrier optionally containing a substrate having an encapsulation coat, where the solid carrier or encapsulation coat contains at least one active agent (I) and one hydrophilic surfactant (II), is new.

ADVANTAGE - The composition is used to deliver a wide variety of active agents having improved absorption and/or biovailability. It provides coated substrate materials without the need for binders. Prior art solid carriers are limited to a few specific drugs due to difficulties in formulating appropriate drug/exicipient compositions to effectively coat the active agent onto a carrier particle. Most of prior art solid dosage forms of hydrophilic active agents exhibit poor or no absorption of the active agent. Non-solid formulations of the same are chemically instable, leak and have capsule shell incompatibility. Conventional solid dosage forms of hydrophobic active agents often exhibit slow and incomplete dissolution and subsequent absorption. They often show a high propensity for biovariability and food interactions of the active agent, resulting in restrictive compliance/labeling requirements. A comparative dissolution study was performed on 3 forms of glyburide (Ia) namely coated beads of (Ia), commercially available (Ia) and pure (Ia) bulk. 5 mg Of each form was usd for triplication dissolution runs in 500 ml of isotonic pH 7.4 phosphate buffer.The dissolutiom medium was sampled at 15, 30, 45, 60, 120 and 180 minutes. The samples were filtered and the filtrates diluted for (Ia)-specific HPLC assay. The (Ia)-coated beads showed a superior dissolution profile in the rate, extent and variability of (Ia) dissolved/released into the medium.

Dwg.0/3

TECH UPTX: 20010910

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: (I) is a drug, a nutrient, a cosmeceutical and/or a diagnostic agent. The substrate may be an additive and/or an active agent. (I) may be hydrophobic having an intrinsic aqueous solubility of less than 1 mg/ml. (I) may be hydrophilic with an apparent water solubility of at least 1 mg/ml. Hydrophilic (I) is selected from a drug, cytokine, peptidomimetic, peptide, protein, toxoid, serum, antibody, vaccine, nucleoside, nucleotide, genetic material and/or nucleic acid. The encapsulation coat further comprises at least one lipophilic additive selected from lipophilic surfactants and/or triglycerides. The composition is encapsulated, extruded, compressed, pelletized, coated, mixed, granulated, crystallized, Iyophilized or molded. It may be formulated as a capsule, a tablet, an ovule, a suppository, a wafer, a chewable tablet, a buccal tablet, a sub-lingual tablet, a quick-dissolve tablet, an effervescent tablet, a granule, a pellet, a bead, a pill, a sachet, a sprinkle, a film, a dry syrup, a reconstitutable solid, a suspension, a lozenge, a troche, an implant, a powder, a triturate, a platelet, or a strip. It may be formulated for immediate release, pulsatile release, controlled release, extended release, delayed release, targeted release, or targeted delayed release.

Preferred Substrate: The substrate is a powder or a multiparticulate. It may be an additive comprising a solubilizer, an enzyme inhibitor, an anti-adherent, an anticoagulant, an antifoaming agent, an antioxidant, a binder, a bufferant, a chelating agent, a coagulant, a colorants or opaquants, a coolant, a cryoprotectant, a diluent or filler, a disintegrant or super disintegrant, a hydrogen bonding agent, a flavorant or desensitizer, an ion-exchange resin, a plasticizer, a preservative, a solvent, a sweetener and/or a thickener. the substrate is a multiparticulate comprised of a granule, a pellet, a bead, a spherule, a beadlet, a microcapsule, a millisphere, a nanocapsule, a nanosphere, a microsphere, a platelet, a tablet or a capsule.

Preferred Carrier: The carrier is a bead, a beadlet, a granule, a spherule, a pellet, a microcapsule, a microsphere, a nanosphere, a film, a wafer, a sprinkle, an implant, a troche, a lozenge, a platelet, a nanocapsule or a strip. It is enteric coated, coated for fast disintegration, seal coated, film coated, barrier coated, compress coated, or coated with an enzyme-degradable coating.

Preferred Lipophilic Additive: The lipophilic additive is selected from alcohols, polyoxyethylene alkylethers, fatty acids, bile acids, glycerol fatty acid esters, acetylated glycerol fatty acid esters, lower alcohol fatty acids esters, polyethylene glycol fatty acids esters, polyethylene glycol glycerol fatty acid esters, polypropylene glycol fatty acid esters, polyoxyethylene glycerides, lactic acid derivatives of mono/diglycerides, propylene glycol diglycerides, sorbitan fatty acid esters, polyoxyethylene sorbitan fatty acid esters, polyoxyethylenepolyoxypropylene block copolymers, transesterified vegetable oils, sterols, sterol derivatives, sugar esters, sugar ethers, sucroglycerides, polyoxyethylene vegetable oils, polyoxyethylene hydrogenated vegetable oils, reaction mixtures of polyols and at least one fatty acid, glyceride, optionally hydrogenated vegetable oils, and/or sterols. The triglyceride is selected vegetable oils, fish oils, animal fats, hydrogenated vegetable oils, partially hydrogenated vegetable oils, synthetic triglycerides, modified triglycerides, and/or fractionated triglycerides.

Preferred Surfactant: (II) is a non-ionic surfactant (IIa) having an hydrophilic-lipophilic balance (HLB) value of at least 10 or an ionic surfactant (IIb). (IIa) is selected from alkylglucosides, alkylmaltosides, alkylthioglucosides, lauryl macrogolglycerides, polyoxyethylene alkyl ethers, alkylphenols, or sorbitan fatty acid esters, polyethylene glycol

glycerol fatty acid esters, polyoxyethylene- polyoxypropylene block copolymers, polyglycerol fatty acid esters, polyoxyethylene glycerides, polyoxyethylene sterols, polyoxyethylene vegetable oils, polyoxyethylene hydrogenated vegetable oils and/or reaction mixtures of polyols and at least one fatty acid, glyceride, vegetable oil, hydrogenated vegetable oil, and sterol, tocopherol polyethylene glycol succinate, sugar ester, sugar ether and/or sucroglycerides. (IIb) is selected from alkyl ammonium salts, bile acids and their salts, or derivatives, fatty acid derivatives of amino acids, carnitines, oligopeptides, and polypeptides, glyceride derivatives of amino acids, oligopeptides, and polypeptides, acyl lactylates, mono-or diacetylated tartaric acid esters of mono- or diglycerides, succinylated monoglycerides, citric acid esters of mono- or diglycerides, alginate salts, propylene glycol alginate, optionally hydrogenated lecithins, optionally hydrogenated lysolecithins, lysophospholipids, phospholipids, alkylsulfate salts, fatty **acid salts** and/or sodium docusate.

TECHNOLOGY FOCUS - POLYMERS - Preferred Surfactant: (II) is a non-ionic surfactant (IIa) having an hydrophilic-lipophilic balance (HLB) value of at least 10 or an ionic surfactant (IIb). (IIa) is selected from alkylglucosides, alkylmaltosides, alkylthioglucosides, lauryl macrogolglycerides, polyoxyethylene alkyl ethers, alkylphenols, or sorbitan fatty acid esters, polyethylene glycol glycerol fatty acid esters, polyoxyethylene- polyoxypropylene block copolymers, polyglycerol fatty acid esters, polyoxyethylene glycerides, polyoxyethylene sterols, polyoxyethylene vegetable oils, polyoxyethylene hydrogenated vegetable oils and/or reaction mixtures of polyols and at least one fatty acid, glyceride, vegetable oil, hydrogenated vegetable oil, and sterol, tocopherol polyethylene glycol succinate, sugar ester, sugar ether and/or sucroglycerides. (IIb) is selected from alkyl ammonium salts, bile acids and their salts, or derivatives, fatty acid derivatives of amino acids, carnitines, oligopeptides, and polypeptides, glyceride derivatives of amino acids, oligopeptides, and polypeptides, acyl lactylates, mono-or diacetylated tartaric acid esters of mono- or diglycerides, succinylated monoglycerides, citric acid esters of mono- or diglycerides, alginate salts, propylene glycol alginate, optionally hydrogenated lecithins, optionally hydrogenated lysolecithins, lysophospholipids, phospholipids, alkylsulfate salts, fatty **acid salts** and/or sodium docusate.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Active Agent: (I) is selected from hydrophobic agents that are analgesics, anti-inflammatory agents, anthelmintics, anti-arrhythmic agents, anti-bacterial agents, anti-viral agents, anti-coagulants, anti-depressants, anti-diabetics, anti-epileptics, anti-fungal agents, anti-gout agents, anti-hypertensive agents, anti-malarials, anti-migraine agents, anti-muscarinic agents, anti-neoplastic agents, erectile dysfunction improvement agents, immunosuppressants, anti-protozoal agents, anti-thyroid agents, anxiolytic agents, sedatives, hypnotics, neuroleptics, D-Blockers, cardiac inotropic agents, corticosteroids, diuretics, anti-parkinsonian agents, gastro-intestinal agents, histamine receptor antagonists, keratolytics, lipidregulating agents, anti-anginal agents, COX-2 inhibitors,leucotriene inhibitors, macrolides, muscle relaxants, nutritional agents, opioid analgesics, protease inhibitors, sex hormones, stimulants, muscle relaxants, anti-osteoporosis agents,anti-obesity agents, cognition enhancers, anti-urinary incontinence agents, nutritional oils, anti-benign prostate hypertrophy agents, essential fatty acids and/or non-essential fatty acids. (I) is selected from acutretin, albendazole, albuterol, aminogluthemide, amiodarone, arniodipine, amphetamine, amphotericin B, atorvastatin, atovaquone, azithromycin, bactofen, beclomethsone, benezepril, benzonatate, betamethasone, bicalutanide, budesonide, bupropion, busulphan, butenafine, calcifediol, calciprotiene, calcitriol,

camptothecan, candesartan, capsaicin, carbamezepine, carotenes, celecoxib, cerivistatin, cetrizine, chlorpheniramine, cholecalciferol, cilostazol, cimetidine, cinnarizine, ciprofloxacin, cisapride, clarithromycin, clemastine, clormphene, clornipramine, clopidrogel, codeine, coenzyme Q10, cyclobenzaprine, cyclosporine, danazol, dantrolene, dexchlopheniramine, diclofenac, dicournarol, digoxin, dihydroepiandrosterone, dihydroergotamine, dihydrotachysterol, dirithromycin, donepezil, efavirenz, eposartan, ergocalciferol, ergotarnine, essential fatty acid sources, etodolac, etoposide, famotidine, fenofibrate, fentanyl, fexofenadine, finasteride, flucanazole, flurbiprofen, fluvastatin, fosphenytion, frovatriptan, furazolidone, **gabapentin**, gemfibrozil, glibenclamide, glipizide, glyburide, glymepride, griseofulvin, halofantrine,lbuprofen, irbesartan, irinotecan, isosorbide dinitrate, isotreinoin, itraconazole, ivermectin, ketoconazoie, ketorolac, lamotrigine, lanosprazole, leflunomide, lisinopril,loperamide, loratadine, lovastatin, L-thryroxine, lutein, lycopene, medroxyprogesterone,mefepristo ne, mefloquine, megesterol acetate, methadone, methoxsalen, metronidazole, metronidazole, miconazole, midazolam, miglitol, minoxidil, mitoxantrone, montelukast, nabumetone, nalbuphine, naratiptan, nelfinavir, nifedipine, nilsolidipine, nilutanide, nitrofurantoin, nizatidine, orneprazole, oprevelkin, osteradiol, oxaprozin, paclitaxel, paricalcitol, paroxetine, pentazocine, pioglitazone, pizofetin, pravastatin, prednisolone, probucol, progesterone, pseudo-ephedrine, pyridostigmine, rabeprazole, raloxifene, refocoxib, repaglinide, rifabutine, rifapentine, rimexolone, ritanovir, rizatriptan, rosigiltazone, saquinavir, sertraline, sibutramine, sildenafil citrate, simvastatin, sirolimus, spironolactone, sumatriptan, tacrine, tacrolimus, tamoxifen, tamsulosin, targretin,tazarotene, telmisartan, teniposide, terbinafine, terzosin, tetrahydrocannabinol, tiagabine,ticlidopine, tirofibran, tizanidine, topiramate, topotecan, toremifene, trarnadol, tretinoin, troglitazone, trovafloxacin, ubidecarenone, valsartan, venlafaxine, vertoporfin, vigabatrin, vitamin A, vitamin D, vitamin E, vitamin K, zafirlukast, zileuton, zolmitriphan, zolpidem and/or zopiclone. (I) may also be selected from acarbose, acylovir, acetylcysteine, acetylcholine chloride, alatrofloxacin, alendronate, alglucerase, amantadine hydrochloride, ambenomium, amifostine, amiloride hydrochloride, aminocaproic acid, amphotericin B, antihemophilic factor (human), antihemophilic factor (porcine), antihemophilic factor (recombinant), aprotinin, asparaginase, atenolol, atracurium besylate, atropine, azithromycin, aztreonam, BCG vaccine, bacitracin, becalermin, belladona, bepridil hydrochloride, bleomycin sulfate, calcitonin human, calcitonin salmon, carboplatin, capecitabine, capreomycin sulfate, cefamandole nafate, cefazolin sodium, cefepime hydrochloride, cefixime, cefonicid sodium, cefoperazone, cefotetan disodium, cefotoxime, cefoxitin sodium, ceftizoxime, ceftriaxone, cefuroxime axetil, cephalexin, cephapirin sodium, cholera vaccine, chrionic gonadotropin, cidofovir, cisplatin, cladribine, clidinium bromide, clindamycin and clindamycin derivatives, ciprofloxacin, clondronate, colistimethate sodium, colistin sulfate, cortocotropin, cosyntropin, cromalyn sodium, cytarabine, daltaperin sodium, danaproid, deforoxamine, denileukin diftitox, desmopressin, diatrizoate megluamine and diatrizoate sodium, dicyclomine, didanosine, dirithromycin, dopamine hydrochloride, domase alpha, doxacurium chloride, doxorubicin, editronate disodium, elanaprilat, enkephalin, enoxacin, enoxaprin sodium, ephedrine, epinephrine, epoetin alpha, erythromycin, esmol hydrochloride, factor IX, famiciclovir, fludarabine, fluoxetine, foscarnet sodium, ganciclovir, granulocyte colony stimulating factor, granulocyte-macrophage stimulating factor, growth hornone-recombinant human, growth hormone-bovine, gentamycin, glucagon, glycopyrolate, gonadotropin releasing hormone and synthetic analogs, GnRH, gonadorelin, grepafloxacin, hemophilus B conjugate vaccine, Hepatitis A virus vaccine inactivated, Hepatitis B

virus vaccine inactivated, heparin sodium, indinavir sulfate-, influenza virus vaccine, interleukin-2, interleukin-3, insulin-human, insulin lispro, insulin procine, insulin NPH, insulin aspart, insulin glargine, insulin detemir, interferon alpha, interferon beta, ipratropium bromide, isofosfamide, japanese encephalitis virus vaccine, lamivudine, leucovorin calcium, leuprolide acetate, levofloxacin, lincomycin and lincomycin derivatives, lobucavir, lomefloxacin, loracarbef, mannitol, measles virus vaccine, meningococcal vaccine, menotropins,mephenzolate bromide, mesalmine, methanamine, methotrexate, methscopolamine, metformin hydrochloride, metroprolol, mezocillin sodium, rnivacurium chloride, mumps, viral vaccine, nedocromil sodium, neostigmine bromide, neostigmine methyl sulfate, neutontin, norfloxacin, octreotide acetate, ofloxacin, olpadronate, oxytocin, pamidronate disodium, pancuronium bromide, paroxetine, pefloxacin, pentarnindine isethionate, pentostatin, pentoxifylllne, periciclovir, pentagastrin, phentolarnine mesylate, phenylalanine, physostigmine salicylate, plague vaccine, piperacillin sodium, platelet derived growth factor-human, pneumococcal vaccine polyvalent, poliovirus vaccine inactivated, pollovirus vaccine live (OPV), polymixin B sulfate, pralidoxine chloride, pramlintide, pregabalin, propofenone, propenthaline bromide, pyridostigmine bromide, rabies vaccine, residronate, ribavarin, rimantadine hydrochloride, rotavirus vaccine, salmetrol xinafoate, sincalide, small pox vaccine, solatol, somatostatin, sparfloxacin, spectinomycin, stavudine, streptokinase, streptozocin, suxamethoniurn chloride, tacrine hydrochloride, terbutaline sulfate, thiopeta, ticarcillin, tiludronate, timolol, tissue type plasminogen activator, TNFR:Fc, TNK-tPA, trandolapril, trimetrexate gluconate, trospectinomycin, trovafloxacin, tubocurarine chloride, tumor necrosis factor, typhoid vaccine live, urea, urokinase, vancomycin, valaciclovir, valsartan, varicella virus vaccine live, vasopressin and vasopressin derivatives, vecoronium bromide, vinblastin, vincristine, vinorelbine, vitamin B12 , warfarin sodium, yellow fever vaccine, zalcitabine, zanamavir, zolandronate, and/or zidovudine.

L11 ANSWER 8 OF 11 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2001-061435 [07] WPIDS
DNC C2001-017005
TI Porous drug matrices, providing enhanced drug dissolution in aqueous media.
DC B05 B07
IN BERNSTEIN, H; CHICKERING, D E; KHATAK, S; RANDALL, G; STRAUB, J; KHATTAK, S; ALTREUTER, D
PA (ACUS-N) ACUSPHERE INC
CYC 92
PI WO 2000072827 A2 20001207 (200107)* EN 45
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000054459 A 20001218 (200118)
EP 1180020 A2 20020220 (200221) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
NO 2001005753 A 20020128 (200225)
US 2002041896 A1 20020411 (200227)
BR 2000010984 A 20020430 (200237)
US 6395300 B1 20020528 (200243)
KR 2002011992 A 20020209 (200257)
US 2002142050 A1 20021003 (200267)

CN 1365274 A 20020821 (200281)
JP 2003500438 W 20030107 (200314) 63
US 6610317 B2 20030826 (200357)
NZ 516083 A 20030829 (200365)
ZA 2001010347 A 20030923 (200368) 66
US 6645528 B1 20031111 (200382)
AU 768022 B 20031127 (200404)
MX 2001012106 A1 20030701 (200420)

ADT WO 2000072827 A2 WO 2000-US14578 20000525; AU 2000054459 A AU 2000-54459 20000525; EP 1180020 A2 EP 2000-939365 20000525, WO 2000-US14578 20000525; NO 2001005753 A WO 2000-US14578 20000525, NO 2001-5753 20011126; US 2002041896 A1 Provisional US 2000-186310P 20000302, US 2001-798824 20010302; BR 2000010984 A BR 2000-10984 20000525, WO 2000-US14578 20000525; US 6395300 B1 Provisional US 1999-136323P 19990527, Provisional US 1999-158659P 19991008, US 1999-433486 19991104; KR 2002011992 A KR 2001-715052 20011124; US 2002142050 A1 Provisional US 1999-136323P 19990527, Provisional US 1999-158659P 19991008, CIP of US 1999-433486 19991104, US 2002-53929 20020122; CN 1365274 A CN 2000-808161 20000525; JP 2003500438 W JP 2000-620939 20000525, WO 2000-US14578 20000525; US 6610317 B2 Provisional US 1999-136323P 19990527, Provisional US 1999-158659P 19991008, Provisional US 2000-186310P 20000302, Cont of WO 2000-US14578 20000525, US 2001-798824 20010302; NZ 516083 A NZ 2000-516083 20000525, WO 2000-US14578 20000525; ZA 2001010347 A ZA 2001-10347 20011218; US 6645528 B1 Provisional US 1999-136323P 19990527, Provisional US 1999-158659P 19991008, Div ex US 1999-433486 19991104, US 2000-694407 20001023; AU 768022 B AU 2000-54459 20000525; MX 2001012106 A1 WO 2000-US14578 20000525, MX 2001-12106 20011126

FDT AU 2000054459 A Based on WO 2000072827; EP 1180020 A2 Based on WO 2000072827; BR 2000010984 A Based on WO 2000072827; US 2002142050 A1 CIP of US 6395300; JP 2003500438 W Based on WO 2000072827; NZ 516083 A Based on WO 2000072827; US 6645528 B1 Div ex US 6395300; AU 768022 B Previous Publ. AU 2000054459, Based on WO 2000072827; MX 2001012106 A1 Based on WO 2000072827

PRAI US 2000-186310P 20000302; US 1999-136323P 19990527;
US 1999-158659P 19991008; US 1999-433486 19991104;
US 2002-53929 20020122; US 2000-694407 20001023

AB WO 200072827 A UPAB: 20011129

NOVELTY - Porous drug matrices enhance drug dissolution in aqueous media.

DETAILED DESCRIPTION - A porous drug matrix is prepared by:

(a) dissolving the drug in a volatile solvent;

(b) combining at least 1 pore forming agent with the drug solution to form an emulsion, suspension or solution; and

(c) removing the volatile solvent and pore forming agent to give the porous matrix of drug.

INDEPENDENT CLAIMS are included for the following:

(a) a composition comprising a porous matrix formed from a wetting agent and microparticles of a drug, where the microparticles have diameter 0.01-5 mu m and total surface area greater than 0.5 m2/ml, and the dry porous matrix is in dry powder form; and

(b) use of the compositions for drug delivery.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - For delivery of drugs. The porous matrix forms nanoparticles and microparticles of the drug on contact with an aqueous medium.

ADVANTAGE - The formulations can be used to convert drugs which must be infused (e.g. to avoid precipitation of the drug following bolus injection) to a bolus formulation, avoiding unacceptable precipitation of the drug in vivo~~, or for local delivery~~.

Dwg.0/9

TECH UPTX: 20010202

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: A wetting agent may be incorporated into the emulsion, suspension or solution in step (b). Further excipients may be included, e.g. hydrophilic polymers, sugars, pegylated excipients (e.g. pegylated phospholipid, shielding the drug from macrophage uptake) and tonicity agents. Step (c) may involve spray drying, evaporation, fluid bed drying, lyophilization and/or vacuum drying. Preferred Drugs: The drug preferably has low aqueous solubility. The drug is chosen from: albuteril, adapalene, budesonide, doxazosin mesylate, mometasone furoate, ursodiol, amphotericin, enalapril **maleate**, felodipine, nefazodone hydrochloride, valrubicin, albendazole, estrogens conjugated, medroxyprogesterone acetate, nicardipine hydrochloride, zolpidem tatrate, amlodipine besylate, ethinyl estradiol, omeprazole, rubitecan, amlodipine besylate/benazepril hydrochloride, etodolac, paroxetine hydrochloride, atovaquone, felodipine, podofilox, paricalcitol, betamethasone dipropionate, fentanyl, pramipexole dihydrochloride, vitamin D3 and related analogues, finasteride, quetiapine fumarate, alpostadil candesartan, cilexetil, fluconazole, ritonavir, busulfan, carbamazepine, flumazenil, risperidone, carbemazepine, carbidopa/levodopa, ganciclovir, saquinavir, amprenavir, carboplatin, glyburide, sertraline hydrochloride, rofecoxib carvedilol, halobetasolproprionate, sildenafil citrate, celecoxib, chlorthalidone, imiquimod, simvastatin, citalopram, ciprofloxacin, irinotecan hydrochloride, sparfloxacin, efavirenz, cisapride monohydrate, lansoprazole, tamsulosin hydrochloride, mofafinil, azithromycin, clarithromycin, letrozole, terbinafine hydrochloride, rosiglitazone **maleate**, diclofenac sodium, lomefloxacin hydrochloride, tirofiban hydrochloride, telmisartan, diazapam, loratadine, toremifene citrate, thalidomide, dinoprostone, mefloquine hydrochloride, trandolapril, mitoxantrone hydrochloride, tretinoin, etodolac, triamcinolone acetate, estradiol, ursodiol, nelfinavir mesylate, indinavir, beclomethasone dipropionate, oxaprozin, flutamide, famotidine, nifedipine, prednisone, cefuroxime, lorazepam, digoxin, lovastatin, griseofulvin, naproxen, ibuprofen, isotretinoin, tamoxifen citrate, nimodipine, amiodarone and alprazolam, ketoconazole, ceftazidime, albuterol sulfate, valacyclovir, urofollitropin, famiciclovir, enalapril, mefformin, itraconazole, buspirone, **gabapentin**, fosinopril, tramadol, acarbose, lorazepan, follitropin, glipizide, fluxetine, lisinopril, levixacin, zafirlukast, interferon, growth hormone, interleukin, erythropoietin, granulocyte stimulating factor, nizatidine, buproppion, perindopril, erbumine, adenosine, alendronate, alprostadil, benazepril, betaxolol, bleomycin sulfate, dexfenfluramine, diltiazem, flecainid, gemcitabine, glatiramer acetate, granisetron, lamivudine, mangafodipir, trisodium, mesalamine, metoprolol fumarate, metronidazole, miglitol, moexipril, monteleukast, octreotide acetate, olopatadine, somatropin, sumatriptan succinate, tacrine, verapamil, nabumetone, trovafloxacin, dolasetron, zidovudine, tobramycin, isradipine, tolcapone, enoxaparin, fluconazole, terbinafine, pamidronate, didanosine, diclofenac, cisapride, venlaxine, troglitazone, fluvastatin, losartan, imiglucerase, donepezil, olanzapine, valsartan, fexofenadine, calcitonin or ipratropium. Taxanes such as paclitaxel or docetaxel are particularly preferred. Water soluble drugs include e.g. ketoconazole, omeprazole or ipratropium. Preferred Compounds: The pore forming agent is a volatile **salt**, e.g. ammonium bicarbonate, acetate, chloride and/or benzoate. Preferred Composition: The composition preferably comprises microparticles of mean diameter 0.01-5 (especially 1-5) mum and a total surface area greater than 0.5 m2/ml. They may be suspended in an aqueous solution for parenteral administration; or the matrix may be processed into tablets or capsules for oral administration; formed into suppositories for vaginal or rectal administration; or used in dry powder form for pulmonary administration. The dry powder form preferably has a TAP density less than or equal to 1.0 g/ml.

L11 ANSWER 9 OF 11 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2001-050079 [06] WPIDS
DNC C2001-013807
TI Controlled release and taste masking oral compositions comprising active ingredient incorporated in a matrix structure.
DC A11 A96 B07
IN AJANI, M; FOSSATI, L; PEDRANI, M; VILLA, R
PA (CIPN-N) CIP-NINETY TWO-92 SA; (COSM-N) COSMO SRL; (COSM-N) COSMO SPA
CYC 94
PI WO 2000076478 A1 20001221 (200106)* EN 25
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000056801 A 20010102 (200121)
EP 1183014 A1 20020306 (200224) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
NO 2001006108 A 20020124 (200225)
CN 1355693 A 20020626 (200263)
IT 1312634 B 20020503 (200279)
JP 2003501457 W 20030114 (200306) 24
IT 1317871 B 20030715 (200358)
EP 1183014 B1 20031008 (200370) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 60005819 E 20031113 (200382)
MX 2001012889 A1 20030601 (200417)
ES 2208349 T3 20040616 (200442)
ADT WO 2000076478 A1 WO 2000-EP5356 20000609; AU 2000056801 A AU 2000-56801 20000609; EP 1183014 A1 EP 2000-942044 20000609, WO 2000-EP5356 20000609; NO 2001006108 A WO 2000-EP5356 20000609, NO 2001-6108 20011214; CN 1355693 A CN 2000-808894 20000609; IT 1312634 B IT 1999-MI1317 19990614; JP 2003501457 W WO 2000-EP5356 20000609, JP 2001-502812 20000609; IT 1317871 B IT 2000-MI422 20000303; EP 1183014 B1 EP 2000-942044 20000609, WO 2000-EP5356 20000609; DE 60005819 E DE 2000-00005819 20000609, EP 2000-942044 20000609, WO 2000-EP5356 20000609; MX 2001012889 A1 WO 2000-EP5356 20000609, MX 2001-12889 20011213; ES 2208349 T3 EP 2000-942044 20000609
FDT AU 2000056801 A Based on WO 2000076478; EP 1183014 A1 Based on WO 2000076478; JP 2003501457 W Based on WO 2000076478; EP 1183014 B1 Based on WO 2000076478; DE 60005819 E Based on EP 1183014, Based on WO 2000076478; MX 2001012889 A1 Based on WO 2000076478; ES 2208349 T3 Based on EP 1183014
PRAI IT 2000-MI422 20000303; IT 1999-MI1317 19990614
AB WO 200076478 A UPAB: 20010126
NOVELTY - Controlled release and taste masking oral compositions comprise active ingredients incorporated in a matrix structure.
DETAILED DESCRIPTION - A controlled release and taste masking oral composition containing an active ingredient comprises:
(a) a matrix consisting of lipophilic compounds with melting point lower than 90 deg. C in which the active ingredient is at least partially dispersed;
(b) optionally an amphiphilic matrix;
(c) an outer hydrophilic matrix in which (a) and (b) are dispersed; and
(d) optionally other excipients.
ACTIVITY - Analgesic; antitussive; bronchodilator, antipsychotic; antiparkinson; antihistamine; antiinflammatory; antidiarrheal;

spasmolytic; anxiolytic; antidiabetic; cathartic; antiepileptic; antimicrobial.

MECHANISM OF ACTION - Selective beta -2 antagonist; calcium antagonist; antihistamine,

USE - For oral administration of active ingredients.

Dwg.0/0

TECH UPTX: 20010126

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Compounds: The lipophilic matrix comprises unsaturated or hydrogenated alcohols or fatty **acids**, **salts**, esters or amides, mono-, di- or triglycerids of fatty acids, the polyethoxylated derivatives, waxes or cholesterol derivatives. The lipophilic matrix preferably comprises 6-20C alcohols or 8-20C fatty acids or esters of fatty acids with glycerol or sorbitol or other polyalcohol having less than 6C in the C chain. The amphiphilic compounds are polar lipids of type I or II (lecithin, phosphatidylcholine, phosphatidylethanolamine), ceramides, glycol alkyl ethers, esters of fatty acids with polyethylene glycols or diethylene glycols. The composition may also contain bioadhesive substances. The hydrophilic matrix consists of hydrogel-forming compounds, e.g. acrylic or methacrylic acid polymers or copolymers, alkylvinyl polymers, hydroxyalkylcellulose, carboxyalkylcellulose, polysaccharides, dextrins, pectins, starches and derivatives, alginic acid, natural or synthetic gums, polyalcohols.

The active ingredient is an analgesic, antitussive, bronchodilator, antipsychotic, selective beta-2 antagonist, calcium antagonist, antiparkinson drug, non-steroidal antiinflammatory drug, antihistamine, antidiarrheal or intestinal antiinflammatory, spasmolytic, anxiolytic, oral antidiabetic, cathartic, antiepileptic or topical antimicrobial. The active agent is mesalazine (5-aminosalicyclic acid), budesonide, metformin, octylonium bromide, **gabapentin**, carbidopa, nimesulide, propionylilcarnitine, isosorbide mono- and dinitrate, naproxen, ibuprofen, ketoprofen, diclofenac, thiaprophenic acid, nimesulide, chlorhexidine, benzydamine, tibezonium iodide, cetylpyridinium chloride, benzalkonium chloride or sodium fluoride.

Preferred Composition: The composition is in the form of tablets, capsules or minitablets, where the active ingredient is wholly contained in the inert/amphiphilic matrix, or is dispersed both in the hydrophilic matrix and in the lipophilic/amphiphilic matrix. Tablets may be chewable or erodible in the buccal cavity or in the first portion of the gastrointestinal tract. The composition may comprise a gastro-resistant coating, e.g. consisting of methacrylic acid polymers or cellulose derivatives.

L11 ANSWER 10 OF 11 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2000-170989 [15] WPIDS
DNC C2000-053125
TI Preparation of pure gabapentin useful for treating epilepsy.
DC B05
IN ARRIGHI, K; PAIOCCHI, M; RUSSO, L; VILLA, M
PA (ZAMB) ZAMBON GROUP SPA
CYC 29
PI WO 2000001660 A1 20000113 (200015)* EN 10
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA CZ HU IL IN KR SI SK US ZA
EP 1095010 A1 20010502 (200125) EN
R: AT BE CH DE DK ES FI FR GB IE IT LI NL PT SE SI
IT 1301528 B 20000623 (200211)
ADT WO 2000001660 A1 WO 1999-EP4289 19990621; EP 1095010 A1 EP 1999-931121 19990621, WO 1999-EP4289 19990621; IT 1301528 B IT 1998-MI1535 19980703
FDT EP 1095010 A1 Based on WO 2000001660

PRAI IT 1998-MI1535 19980703
AB WO 200001660 A UPAB: 20000323
NOVELTY - Preparation of pure gabapentin in anhydrous form comprising the addition of 2-methoxyethanol or 2-ethoxyethanol to an aqueous gabapentin suspension and **crystallizing** with an alcoholic solvent, is new.
DETAILED DESCRIPTION - Preparation of pure gabapentin in anhydrous form comprises:
(a) adding 2-methoxyethanol or 2-ethoxyethanol to an aqueous gabapentin suspension;
(b) removing water by azeotropic distillation to give a suspension containing 20-30 weight% water w.r.t. gabapentin;
(c) diluting with an alcoholic solvent and cooling to -10 to 10 deg. C; and
(d) filtering and drying the **crystalline** gabapentin.
ACTIVITY - Anti-epileptic.
USE - Gabapentin (1-(aminomethyl)cyclohexanacetic acid) is a known anti-epileptic drug (see US4024175).
ADVANTAGE - The process gives highly pure anhydrous gabapentin, with a low content of residual solvents (lower than 100 ppm). It avoids complete water removal and the use of monohydrate gabapentin. It is reproducible at industrial level because during the concentration phase, the mass can be always easily stirred. The amount of solvent used is reduced. Yields are greater than 90%, even in the presence of water higher than 30 w/w% w.r.t gabapentin.
Dwg.0/0
TECH UPTX: 20000323
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: 2-Methoxyethanol is preferably used. 2-Methoxy- or 2-ethoxy-ethanol are used in amounts of 2-5 (preferably 2-3) times the amount by weight of **gabapentin.** (b) is carried out a 40-50 degreesC and 50-80 mmHg. The solvent is selected from MeOH, EtOH, n-PrOH, i-PrOH (preferred), n-BuOH, I-BuOH, sec-BuOH and/or tert.-BuOH and it is used in an amount of 4-10 times by weight w.r.t. **gabapentin.** In (c), cooling is at -5 to 50 degreesC. The process further comprises the preparation of a **gabapentin** solution by elution of a **gabapentin** **salt** solution through a Relite EXA10 resin, to obtain an aqueous **gabapentin** solution at 30-40 wt.%.

L11 ANSWER 11 OF 11 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 1991-059511 [09] WPIDS
DNC C1991-025116
TI High yield 1-aminomethyl-1-cyclohexane acetic acid production - in five stages from cyclohexanone, useful for treating cerebral disorders, e.g. epilepsy.
DC B05
IN GEIBEL, W; HARTENSTEI, J; HERRMANN, W; WITZKE, J; HARTENSTEIN, J
PA (WARN) GOEDECKE AG
CYC 19
PI EP 414274 A 19910227 (199109)* 12
R: AT BE CH DE ES FR GB GR IT LI LU NL SE
DE 3928182 A 19910228 (199110)
HU 54623 T 19910328 (199117)
FI 9004203 A 19910226 (199121)
JP 03118355 A 19910520 (199126)
US 5091567 A 19920225 (199211) 6
HU 207284 B 19930329 (199316)
EP 414274 B1 19930623 (199325) GE 12
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
DE 59001851 G 19930729 (199331)
ES 2058707 T3 19941101 (199444)
IL 95479 A 19960912 (199644)

JP 2846084 B2 19990113 (199907) 9
FI 103040 B1 19990415 (199922)
ADT EP 414274 A EP 1990-116292 19900824; DE 3928182 A DE 1989-3928182 19890825; JP 03118355 A JP 1990-221421 19900824; US 5091567 A US 1990-570487 19900821; HU 207284 B HU 1990-5332 19900824; EP 414274 B1 EP 1990-116292 19900824; DE 59001851 G DE 1990-501851 19900824, EP 1990-116292 19900824; ES 2058707 T3 EP 1990-116292 19900824; IL 95479 A IL 1990-95479 19900823; JP 2846084 B2 JP 1990-221421 19900824; FI 103040 B1 FI 1990-4203 19900824
FDT HU 207284 B Previous Publ. HU 54623; DE 59001851 G Based on EP 414274; ES 2058707 T3 Based on EP 414274; JP 2846084 B2 Previous Publ. JP 03118355; FI 103040 B1 Previous Publ. FI 9004203
PRAI DE 1989-3928182 19890825
AB EP 414274 A UPAB: 19930928
Production of 1-aminomethyl-1- cycloahexane-acetic acid (I) comprises, (1) reacting cyclohexanone with a phosphonate ester (EtO2POCH2COOR to form cyclohexylidene-acetate ester (II) (2) reacting this with MeNo2 to form 1-nitromethyl 1cyclohexane-acetate ester (III), (3) reduction of this to ester (Ia) and spiro cpd. (IV) (4) treating these cpds. with dilute acid to form a (I) salt which (5) is converted to (I) free base using an ion exchanger.
R is ester residue.
USE/ADVANTAGE - (I:gabapentin) is known for treatment of cerebral diseases e.g. epilepsy or vertigo. Compared with known methods, this process involves fewer stages (each taking 4 hr. at most), provides higher yield (50% overall compared with 30%), is less expensive is operable on a large scale, is less hazardous (no formation of explosive azide) and gives a prod. of better than 95% purity, eliminating need for subsequent purifcn.
0/0

L12 ANSWER 1 OF 7 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2004-661862 [64] WPIDS
DNC C2004-236312
TI Transmucosal delivery composition comprises an ionizable pharmaceutical agent (e.g. antihypertensive agent and analgesic) and one or more complementary lipophilic species.
DC A96 B05 B07
IN MCCARTY, J A
PA (PHAR-N) THARM PRODN INC
CYC 108
PI WO 2004075877 A1 20040910 (200464)* EN 68
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
ADT WO 2004075877 A1 WO 2004-US5490 20040224
PRAI US 2003-449647P 20030224
AB WO2004075877 A UPAB: 20041006
NOVELTY - Composition (A) comprises an ionizable pharmaceutical agent (1) and one or more complementary lipophilic species (2) formulated in a transmucosal dosage form.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for transmucosal delivery of (1) comprising admixing (1) with one or more complementary (2) to form a lipophilic association (LA),

formulating the LA in a transmucosal dosage form and administering the transmucosal dosage form to a targeted mucosal membrane in order to deliver (1) through the mucosal membrane and into systemic circulation.

ACTIVITY - Hypotensive; analgesic; antidepressant; anesthetic; antiarrhythmic; antiarthritic; antispasmodic; respiratory-gen.; antianginal; uropathic; antidiabetic; hypertensive; antiparkinsonian; cytostatic; immunosuppressive; antiemetic; antibacterial; fungicide; virucide; antimuscarinic; antiallergic; tranquilizer; sedative; neuroleptic; osteopathic; cardioactive; antilipemic; antimalarial; anticonvulsant; antihelmintic; antismoking; antitussive; gastrointestinal-gen.; muscle relaxant; anorectic; antithyroid; antimigraine.

MECHANISM OF ACTION - Angiotensin-converting-enzyme-inhibitor; opioid agonist.

USE - (A) is useful for transmucosal delivery of (1) (claimed). No biological data given.

Dwg.0/6

TECH UPTX: 20041006

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: (1) is hydrogen-bonded or ion-paired to (2) forming a lipophilic association (LA). (A) further comprises a solvent (ethanol, ethyl acetate, isopropyl alcohol, triacetin, triethyl citrate, tributyl citrate, a polyethylene glycol, propylene glycol, bisabolol, glycerin, mineral oil, ethyl oleate, a fatty acid ester, squalane, an animal oil, a vegetable oil, a hydrogenated vegetable oil, isopropyl myristate, isopropyl palmitate, glycofurol, a terpene, an essential oil, an alcohol, a polyol, a silicone fluid or a glyceride) having a dielectric constant less than that of water (where the LA is solvated in the solvent to form a solubilized LA), a carrier (a silica or a silicified microcrystalline cellulose) (where the LA is adsorbed or absorbed to the carrier), a water-soluble excipient (sugar, polyol, alcohol, saccharide, polysaccharide, glycerin, propylene glycol, ethanol, isopropyl alcohol, ethyl acetate, triacetin, triethyl citrate, tributyl citrate, a dextrate, dextrin, dextrose, fructose, lactitol, lactose, erythritol, maltose, maltitol, maltodextrin, polydextrose, trehalose, mannitol, polyethylene glycol, sorbitol, sucrose or xylitol) possessing a dielectric constant less than the dielectric constant of water, a buffering agent (phosphate, carbonate, tartrate, borate, citrate, acetate or **maleate**), colorant, flavoring, solvent, co-solvent, coating agent, binder, diluent, carrier, disintegrant, glident, lubricant, opacifying agent, humectant, granulating agent, gelling agent, polishing agent, suspending agent, sweetening agent, anti-adherent, preservative, emulsifying agent, antioxidant, levigating agent, plasticizer, surfactant, tonicity agent, viscosity agent, enteric agent, enteric coating, controlled-release agent or coating, wax, wetting agent, thickening agent, suppository base, stiffing agent, stabilizing agent, solubilizing agent, sequestering agent, ointment base, oleaginous vehicle, film-forming agent, essential oil, emollient, dissolution enhancer, dispersing agent and/or cryoprotectant. The carrier is capable of forming an inclusion complex with the LA or solubilized LA. The molar ratio of (2) to (1) is at least about 1:1. (1) possesses an acidic or a basic functional group and (2) is an acid (i) (fatty acid, a long-chain alkyl sulfonic acid or a long chain alkyl sulfuric acid) or a base (preferably cetrimide, oleamidopropyl dimethylamine, didecyldimethyl ammonium chloride, a quaternary surfactant, cetylpyridinium chloride, hexetidine, benzalkonium chloride or an amine or amide of (i)). (1) is dihydroergotamine, fentanyl, sufentanil, lidocaine, alfentanil, lofentanil, carfentanil, pentobarbital, buspirone, ergotamine, bisphosphonate, alendronic acid, nalbuphine, bupropion, metformin, diethylcarbamazine, tramadol, heparin or a heparin derivative, amoxicillin, **gabapentin**, omeprazole, aspirin, prostaglandin,

methylsergide, ergonovine, endorphins, enkephalins, oxytocin, opiates, heparin and its derivatives, clorazepic acid, barbiturate, albuterol, atropine, scopolamine, selegiline, timolol, nicotine (preferred), cocaine, novocaine, amphetamines, caffeine, methylphenidate, chlorpromazine, ketamine, epinephrine, estropipate, naloxone, naltrexone, furosemide, labetalol, metoprolol, nadolol, isoproterenol, terbutaline, sumatriptan, bupivacaine, prilocaine, loratadine, chloropheniramine, clonidine or tetracaine. (1) is a antihypertensive agent, analgesic, antidepressant, opioid agonist, anesthetic, antiarrhythmic, antiarthritic, antispasmodic, ACE inhibitor, decongestant, antibiotic, antihistamine, anti-anginal, diuretic, anti-hypotensive agent, anti-Parkinson agent, bronchodilator, oxytocic agent, anti-diuretic, anti-hyperglycemic, antineoplastic and/or immunosuppresent agent, antiemetic, antiinfective, antifungal, antiviral, antimuscarinic, antidiabetic agent, antiallergy agent, anxiolytic, sedative, antipsychotic, bone modulating agent, cardiovascular agent, cholesterol lowering drug, antimalarial, antiepileptic, antihelminthic, agent for smoking cessation, cough suppressant, expectorant, mucolytic, nasal decongestant, dopaminergic, gastrointestinal agent, muscle relaxant, neuromuscular blocker, parasympathomimetic, prostaglandin, stimulant, anorectic, thyroid or antithyroid agent, hormone, antimigraine agent, antiobesity and/or non-steroidal anti-inflammatory agent. (A) is prepared as a buccal tablet, sublingual tablet, oral capsule, oral tablet, nasal spray, buccal or vaginal spray, liquid/semisolid, aerosol for nasal, buccal or pulmonary delivery, patch, lozenge, gum, lollypop, film, strip, paper, suppository or pessary dosage form. (A), when dissolved in water, has a pH of about or near the physiological pH of a target mucosal membrane.

Preferred Method: Admixing (1) with (2) is performed under conditions such that (1) hydrogen-bonds or ion-pairs with (2). The method further comprising solubilizing the LA with a solvent having a dielectric constant less than that of water to form a solubilized LA. (1) is delivered rapidly across the mucosal membrane (oral mucosa, esophagus, gastrointestinal tract, lungs, rectum, sinuses, eye, urinary tract or a lining of a female reproductive organ) in about 10 minutes or less. The dosage form is manufactured by direct tablet compression, wet or dry granulation, dry powder blends, molding, spray-congealing, powder layering, tableting, encapsulating, spray-drying, spheronization, triturates, lyophilization, freeze drying, co-melt, microencapsulation, troching, pelleting, aerosolizing, liquid or semisolid processes. The nicotine is transmucosally delivered sublingually at a pH between 5.5 and 7.5.

L12 ANSWER 2 OF 7 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2003-482240 [45] WPIDS
DNC C2003-128968
TI Pharmaceutical composition useful for the treatment of e.g. depression comprises enantiomerically enriched desmethylcitalopram and/or didesmethylcitalopram as e.g. serotonin reuptake inhibitors.
DC B02
IN BUSH, L R; CURRIE, M G; FANG, K; SENANAYAKE, C H; FANG, Q K; FANG, K Q
PA (SEPR-N) SEPRACOR INC
CYC 101
PI WO 2003040121 A1 20030515 (200345)* EN 29
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
EP 1446396 A1 20040818 (200454) EN

R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
BR 2002013949 A 20040831 (200460)
AU 2002356903 A1 20030519 (200464)
ADT WO 2003040121 A1 WO 2002-US35408 20021105; EP 1446396 A1 EP 2002-802848 20021105, WO 2002-US35408 20021105; BR 2002013949 A BR 2002-13949 20021105, WO 2002-US35408 20021105; AU 2002356903 A1 AU 2002-356903 20021105
FDT EP 1446396 A1 Based on WO 2003040121; BR 2002013949 A Based on WO 2003040121; AU 2002356903 A1 Based on WO 2003040121
PRAI US 2001-337608P 20011108
AB WO2003040121 A UPAB: 20030716
NOVELTY - A pharmaceutical composition (C) contains enantiomerically pure (-)-desmethylcitalopram or enantiomerically enriched (-)-didesmethylcitalopram and/or (+)-didesmethylcitalopram, their salts, solvates or clathrates and an excipient.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(a) a kit comprising the composition and at least one agent (A1) selected from anticonvulsant, psychostimulant, mood stabilizing agent or central nicotine stimulating agent for co-administration with (C);

(b) a racemic, enantiomerically enriched or optically pure form of 1-4(fluorophenyl)-1-(3-oxopropyl)-1,3-dihydro-isobenzofuran-5-carbonitrile (i) and 4-(3-(1,3)-dioxolan-2-yl-1-(4-fluorophenyl)-1-hydroxypropyl)-3-hydroxymethylbenzonitrile (ii);

(c) a method of synthesizing (-)-desmethylcitalopram comprising:

(1) reacting 5-cyanophthalide with 4-fluorophenyl magnesium bromide in the presence of a chiral ligand, followed by reaction with a second Grignard reagent prepared by reacting 2-bromoethyldioxolane with magnesium to give (-)-4-(3-(1,3)-dioxolan-2-yl-1-(4-fluorophenyl)-1-hydroxypropyl)-3-hydroxymethylbenzonitrile (iii);

(2) reacting (iii) with mesyl chloride followed by acidic treatment to form (-)-1-4(fluorophenyl)-1-(3-oxopropyl)-1,3-dihydro-isobenzofuran-5-carbonitrile (iv); and

(3) reducing (iv) with sodium borohydride in the presence of methylamine;

(d) a method of synthesizing (-)-didesmethylcitalopram or (+)-didesmethylcitalopram comprising reacting (iv) or (+)-1-4(fluorophenyl)-1-(3-oxopropyl)-1,3-dihydro-isobenzofuran-5-carbonitrile (v) with (+)-tert-butylsulfinamide or (-)-tert-butylsulfinamide in the presence of Ti(OEt)4 to give optically pure or enantiomerically enriched 2-methyl-propane-2-sulfinic acid (3-(5-cyano-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-1-yl)-propylidene)amide (vi); and

(e) a method for treating one or more disorders, dysfunctions or diseases for which serotonin reuptake inhibition is beneficial, comprising the administration of (C).

ACTIVITY - Antidepressant; Tranquilizer; Nootropic; Antimanic; Anorectic; Antiaddictive; Vasotropic; Cerebroprotective; Antiarteriosclerotic; Hemostatic; Anticoagulant; Cardiant; Antianginal; Antiinfertility.

MECHANISM OF ACTION - Muscarine Receptor Binding Inhibitor; Serotonin Reuptake Inhibitor.

(+)-Desmethylcitalopram (A) was tested for its ability to inhibit the reuptake of radiolabeled serotonin into synaptosomes prepared from various regions of rat brain.

(A) showed 5-HT uptake (IC50) value of 5.8 nM.

USE - (C) is used for treating disorders, dysfunctions or diseases for which serotonin reuptake inhibition is beneficial (e.g. depression, anxiety disorder, attention deficit disorder, attention deficit disorder with hyperactivity, bipolar and manic conditions, bulimia, obesity or weight gain, narcolepsy, chronic fatigue syndrome, seasonal affective

disorder, premenstrual syndrome, substance addiction or abuse and nicotine addiction); for reducing clinical symptoms of affective disorders (e.g. dysphoric mood or pervasive loss of interest or pleasure, associated with symptoms e.g. sleep and appetite disturbances, loss of energy, diminishment of sex drive, onset of body aches or pains, memory loss, inability to make decisions, feelings of self-reproach or excessive or guilt, suicidal thoughts and reduced ability to concentrate); reactive depression, endogenous depression or manic depression; sexual dysfunction, eating disorder, substance abuse, cerebrovascular disorder, vascular disorder, obsessive-compulsive disease, dementia, canine affective aggression, premature ejaculation or erectile dysfunction and anorexia nervosa; for preventing symptoms caused by withdrawal or partial withdrawal from use of tobacco or nicotine; cerebrovascular disorder caused by cerebral infarction, cerebral hemorrhage, cerebral arteriosclerosis, subarachnoid hemorrhage, cerebral thrombosis, cerebral embolism, amnesia and multi infarct dementia; vascular disorder (e.g. myocardial infarction, angina, stroke, pulmonary embolism, transient ischemic attack, deep vein thrombosis, thrombotic reocculusion subsequent to a coronary intervention procedure, heart surgery or vascular surgery, peripheral vascular thrombosis, Syndrome X and heart failure); and disorder in which a narrowing of at least one coronary artery occurs and vascular event (all claimed).

ADVANTAGE - The composition (C) possess potent serotonin reuptake inhibitory activity with minimal inhibitory effects on the reuptake of other known monoamines e.g. norepinephrine (NE) or dopamine (DA). The method achieves the enantiomerically enrichment of greater than 80 (preferably greater than 90, especially greater than 95, particularly greater than 99) %.

Dwg.0/0

TECH UPTX: 20030716

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Component: (A1) is a substrate for a cytochrome P450 enzyme (preferably CYP1A2, CYP2C9, CYP2C19, CYP2D6 or CYP3A4), clozapine, theophylline, warfarin, imipramine, mephenytoin, sparteine, amitriptyline, carbamazepine, triazolam, benzodiazepine, risperidone, **gabapentin** or lamotrigine.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: The resultant amine is isolated or is subsequently reacted with an acid to form a salt. The column chromatography with chiral solid support is used to separate the enantiomers of final or intermediate products.

Preferred Component: The acid is D-**tartaric** acid, L-**tartaric** acid, hydrochloric acid (HCl) or hydrobromic acid (HBr).

L12 ANSWER 3 OF 7 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2003-481871 [45] WPIDS
DNC C2003-128607
TI Production of cationic non-viral delivery vehicle useful e.g. for DNA lipofection or targeted drug delivery, by conjugating steroid or other drug with polyamine and mixing with lipid.
DC A96 B04 B07 D16
IN DIAMOND, S L; GRUNEICH, J
PA (UYPE-N) UNIV PENNSYLVANIA
CYC 101
PI WO 2003015757 A1 20030227 (200345)* EN 70
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM

ZW
EP 1424998 A1 20040609 (200438) EN
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
AU 2002324723 A1 20030303 (200452)
ADT WO 2003015757 A1 WO 2002-US26152 20020815; EP 1424998 A1 EP 2002-759383 20020815, WO 2002-US26152 20020815; AU 2002324723 A1 AU 2002-324723 20020815
FDT EP 1424998 A1 Based on WO 2003015757; AU 2002324723 A1 Based on WO 2003015757
PRAI US 2002-358138P 20020220; US 2001-312729P 20010816
AB WO2003015757 A UPAB: 20030716
NOVELTY - Production of a cationic non-viral delivery vehicle (A) comprises:

(a) mixing an optionally modified or derivatized steroid (or other drug) (I), a polyamine (II), a conjugating reagent (III) and preferably dimethyl sulfoxide (DMSO), so that (I) is conjugated with (II) by (III);

(b) purifying the (I)-(II) conjugate; and

(c) mixing the conjugate with a lipid (IV).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) (A) prepared as above;

(2) a cationic non-viral delivery vehicle comprising a dexamethasone-spermine molecule and (IV);

(3) methods for facilitating the delivery of compounds to cells or tissues, treating diseases or disorders or facilitating incorporation of compounds into cells, all using (A) (where the mixture in (a) includes DMSO) as delivery vehicle for the compounds, and

(4) kits including (A) (where the mixture in (a) includes DMSO) for administration of (A) or treatment of diseases or disorders.

USE - (A) binds with anionic tissue regions (specifically an anionic domain of a glycosaminoglycan, collagen, fibrin, cellular or erythrocyte glycocalyx, sialic acid, sulfated glycocalyx or isolated nucleic acid), and is useful for delivery of active compounds to tissues (specifically muscle, mucosa, epithelial, nerve, connective, blood, stromal, heart, liver, kidney, skin, brain, intestinal, interstitial space, bone, bone marrow, joint, cartilage, tendon, esophagus, gonad, cerebrospinal fluid, pancreas, spleen, ocular, nasal cavity or hair tissue) or to cells (specifically mammalian cells, especially human endothelial, mesenchymal or neural cells, fibroblasts, neurons, smooth muscle, kidney or liver cells, myoblasts, embryonic, hematopoietic or other stem cells, osteoblasts, chondrocytes, chondroblasts, monocytes, neutrophils, macrophages, retinal nerve cells or epithelial cells), in vivo or in vitro (all claimed). In particular, (A) are used in the treatment of inflammation, asthma, arthritis, pain, joint inflammation, cancer, allergy, hypertension, hyperplasia, mestasis, claudication, intimal hyperplasia, hemophilia, coagulopathy, autoimmune disorders, ulcers, erosive esophagitis, heart disorders, pathological hypersecretion, rhinitis, chronic idiopathic urticaria, heartburn, infections, familial adenomatous polyposis, depression, obsessive-compulsive disorder, bulimia nervosa, premenstrual dysphoric disorder, psychosis, schizophrenia, bipolar disorders, generalized or social anxiety disorder, panic, dysmenorrhea, post-traumatic stress, anemia, menopausal symptoms, osteoporosis, hypoestrogenism, kraurosis vulvae, hypercholesterolemia, type II diabetes, Kaposi sarcoma, warts, hepatitis C or B, erectile dysfunction, epilepsy, Paget's disease, neutropenia, progenitor cell mobilization, organ transplant rejection, cluster headache, migraine, angina, hypertension, candidiasis, gastritis, cardiac ischemia complications, endometriosis, central precocious puberty, bronchospasm, gastro-esophageal reflux, mastocytosis or proliferative disorders.

Typically (A) are used in DNA lipofection.

ADVANTAGE - (A) can be prepared by a one-step method, produce high levels of incorporation in cells or tissues and have good targeting and/or slow release properties.

Dwg.0/6

TECH UPTX: 20030716

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (I) Comprises a glucocorticoid, mineralocorticoid, androgen, estrogen, gestagen, analog with steroidal agonist or antagonist activity, inactive structural analog, cationic steroid or cationic steroid prodrug, especially dexamethasone, 11-deoxycorticosterone-21-mesylate, corticosterone-21-mesylate, 11-deoxycortisol-21-mesylate, cortisol-21-mesylate, tamoxifen, 4-hydroxy-tamoxifen, 21-chloro-17-hydroxyprogesterone, cholesterol tosylate, hydrocortisone mesylate, 17alpha-mesylate-estradiol-3-acetate or dexamethasone-21-mesylate; or more generally a hydrophobic drug, drug mesylate derivative, cationic drug or cationic prodrug.

(II) Comprises spermine, a polylysine, lysine, a peptide containing lysine or arginine, a cationic polymer (especially polyethyleneimine) or an amine-rich polymer. (III) Comprises 2-iminothiolane. (IV) Comprises a neutral lipid (specifically dioleoyl phosphatidyl ethanolamine, phosphatidyl choline or cholesterol), a helper lipid or a cationic lipid (specifically 3beta-(N',N'-dimethylaminoethane)-carbamoyl)-cholesterol, N-(1-(2,3-dioleyloxy)-propyl)-N,N,N-triethylammonium, 2'-(1'',2''-dioleoyloxypropyl-dimethylammonium bromide)-N-ethyl-6-aminospermine tetra-trifluoroacetate, 1,3-bis-(oleoyloxy)-3-(trimethylammonio)-propane or GL-67).

The active compound to be delivered using (A) is a nucleic acid (especially a plasmid, expression vector, antisense or other oligonucleotide, PCR product, DNA-RNA chimera, peptide nucleic acid, RNA interference or isolated nucleic acid, particularly DNA), recombinant protein, erythropoietin, tissue plasminogen activator, tumor necrosis factor-alpha receptor, omeprazole, simvistatin, atorvastatin calcium, amlodipine besylate, loratadine, lansoprazole, epoetin-alpha, celecoxib, fluoxetine hydrochloride, olanzapine, paroxetine hydrochloride, rofecoxib, sertraline hydrochloride, a conjugated estrogen, amoxicillin/potassium clavulanate, pravastatin sodium, enalapril **maleate**, metformin hydrochloride, pravastatin, losartan potassium, ciprofloxacin hydrochloride, risperidone, paclitaxel, azithromycin, interferon-alpha-2b, rebavirin, sildenafil citrate, **gabapentin**, flucatisone propionate, alendronate sodium, clarithromycin, filgrastim, cyclosporine, lisinopril dihydrate, venlafaxine hydrochloride, human insulin, levofloxacin, fexofenadine hydrochloride, lisinopril, sumatriptan succinate, nifedipine, fluconazole, ceftriaxone sodium, famotidine, enoxaparin sodium, leuprolide acetate, salmeterol xinafoate, clopidogrel bisulfate or ranitidine.

TECHNOLOGY FOCUS - POLYMERS - Preferred Materials: The polyamines (II) include polylysine, cationic polymers (especially polyethyleneimine) or amine-rich polymers.

L12 ANSWER 4 OF 7 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2003-289895 [28] WPIDS
DNC C2003-075225
TI New method for improving neurological function by administering imidazole derivatives.
DC B03
IN CHEZ, M G
PA (CARN-N) CARN AWARE LLC
CYC 100
PI WO 2003013514 A1 20030220 (200328)* EN 74

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

AU 2002355388 A1 20030224 (200460)

ADT WO 2003013514 A1 WO 2002-US22341 20020715; AU 2002355388 A1 AU 2002-355388 20020715

FDT AU 2002355388 A1 Based on WO 2003013514

PRAI US 2001-325136P 20010927; US 2001-310710P 20010808

AB WO2003013514 A UPAB: 20030501

NOVELTY - New method for improving neurological function by administering imidazole derivatives to patients having e.g. autism, epilepsy and seizures.

DETAILED DESCRIPTION - Method of improving neurological function comprises:

(1) identifying patients having at least one of autism, epilepsy, seizures, pervasive development disorder, cerebral palsy, Tourette's syndrome, attention deficit disorder, attention deficit hyperactive disorder, central auditory processing disorder, dyslexia, aprazia of speech, motor type apraxia, panic disorder, bipolar disorder and/or Asperger's syndrome; and

(2) administering an imidazole derivative (I) or its salt, hydrate or prodrug.

Y = CO or SO2;

R1, R2 = H or Me;

provided that R1 = absent;

when R2 = present;

and vice versa R3 = COOH or H;

R4 = H;

R5, R6 = H or COMe;

provided that one of R5 and R6 = H and the other is COMe;

and n = 1-2.

INDEPENDENT CLAIMS are also included for:

(1) the use of a composition containing (I) for the treatment of the above conditions.

(2) a method of increasing the efficacy of a second active agent (II) comprising an anticonvulsant, selective serotonin reuptake inhibitor medication, acetyl cholinesterase medication, pervasive developmental disorder medication, attention deficit/attention deficit hyperactivity disorder medication or a stimulant comprising administration of (I) to patients having epilepsy or seizure disorders.

(3) a unit dose comprising (I) and (II) (not in admixture) packaged together for co-administration.

ACTIVITY - Nootropic; Anticonvulsant; Cerebroprotective; Neuroleptic; Tranquilizer; Auditory.

MECHANISM OF ACTION - Selective Serotonin Reuptake Inhibitor.

USE - For improving neurological function and treating autism, epilepsy, seizures, pervasive development disorder, cerebral palsy, Tourette's syndrome, attention deficit disorder, attention deficit hyperactive disorder, central auditory processing disorder, dyslexia, aprazia of speech, motor type apraxia, panic disorder, bipolar disorder and/or Asperger's syndrome and general cognitive problems. The compounds are useful for enhancing the efficacy of anticonvulsant, selective serotonin reuptake inhibitor medication, acetyl cholinesterase medication, pervasive developmental disorder medication, attention deficit/attention deficit hyperactivity disorder medication or stimulants in patients suffering from epilepsy and seizure disorders.

Dwg.0/0
TECH UPTX: 20030501
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (I) is preferably carnosine, homocarnosine, anserine, ophidine, carcinine, N-acetyl-carsonine, N-acetyl-homocarsonine, N-acetyl-anserine, N-acetyl-ophidine or N-acetyl-carnicine.
Preferred Composition: The medicament further comprises at least one anticonvulsant (preferably carbamazepine, phenytoin, mephenytoin, ethotoin, mephobarbital, Phenobarbital, primidone, valproate, **gabapentin**, lamotrigine, clonazepam, clorazepate, diazepam, lorazepam, ethosuximide, trimethadione, gamma-vinyl GABA, GABA, acetazolamide, felbamate, tiagabine, levetiracetam, vigabatrin and/or topiramate), selective serotonin reuptake inhibitor (preferably clomipramine hydrochloride, citalopram hydrobromide, venlafaxine hydrochloride, fluvoxamine **maleate**, paroxetine hydrochloride, fluoxetine hydrochloride and/or sertraline hydrochloride), acetyl cholinesterase medication (preferably donepezil hydrochloride , rivastigmine and/or galantamine), pervasive developmental disorder medication (preferably an anticonvulsant, selective serotonin reuptake inhibitor and/or acetyl cholinesterase inhibitor), attention deficit/attention deficit hyperactivity disorder medication (preferably atomoxetine, clonidine, dextroamphetamine, pemoline and/or methylphenidate) and/or a stimulant (preferably amineptine, amphetamine, amphtaminil, bemegride, benphetamine, brucine, caffeine, chlorphentermine, clofenciclan, clortermine, coca, demanyl phosphate, deoxadrol, dextroamphetamine sulfate, N-ethylamphetamine, ethamivan, etifelmin, etryptamine, fencamfamine, fenethylline, fenozolone, flurothyl, hexacyclonate sodium, homocamfin, mazindol, mefexamide, methamphetamine, methylphenidate, nikethamide, pemoline, pentylenetetrazole, phendimetrazine, phenmetrazine, phentermine, picrotoxin, pipradrol, prolintane or pyrovalerone).

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: The composition preferably comprises carnosine and a metal ion comprising zinc, copper and/or iron and vitamin B6 or vitamin E.

L12 ANSWER 5 OF 7 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2003-229326 [22] WPIDS
DNC C2003-058884
TI New nitrooxy derivatives used for treating pain.
DC B05
IN DEL SOLDATO, P; ONGINI, E
PA (NICO-N) NICOX SA; (DSOL-I) DEL SOLDATO P; (ONGI-I) ONGINI E
CYC 92
PI WO 2003000642 A2 20030103 (200322)* EN 31
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AU BA BB BG BR BZ CA CN CO CR CU CZ DM DZ EC EE GD GE HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX NO NZ OM PH PL RO SG SI SK TN TR TT UA US UZ VN YU ZA
EP 1417165 A2 20040512 (200431) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2004171682 A1 20040902 (200458)
AU 2002344965 A1 20030108 (200461)
ADT WO 2003000642 A2 WO 2002-EP5166 20020510; EP 1417165 A2 EP 2002-742986 20020510, WO 2002-EP5166 20020510; US 2004171682 A1 WO 2002-EP5166 20020510, US 2003-480805 20031219; AU 2002344965 A1 AU 2002-344965 20020510
FDT EP 1417165 A2 Based on WO 2003000642; AU 2002344965 A1 Based on WO

2003000642
PRAI IT 2001-MI1308 20010621
AB WO2003000642 A UPAB: 20030402
NOVELTY - Nitrooxy derivatives (I) are new.
DETAILED DESCRIPTION - Nitrooxy derivatives of formula A-(B)ba-(C1)ca-NO2 (I) or their salts are new.
ba, ca = 0 or 1 (preferably 1);
A = R-T1;
R = radical of an analgesic drug for chronic pain (preferably for neuropathic pain);
T1 = (CO)t or (X)t';
X = O, S or NR1c;
R1c = H or 1-5C alkyl;
B = Tb-X2-Tb1;
precursor compound of B = L-carnosine, anserine, selenocysteine, selenomethionine, penicillamine, N-acetylpenicillamine, cysteine, N-acetylcysteine, glutathione or their ester (preferably ethyl or isopropyl ester), gallic acid, ferulic acid, gentisic acid, citric acid, caffeic acid, dihydrocaffeic acid, p-cumaric acid, vanillic acid, nordihydroguaiaretic acid, quercetin, catechin, kaempferol, sulfurethyne, ascorbic acid, isoascorbic acid, hydroquinone, gossypol, reductic acid, methoxy hydroquinone, hydroxyhydroquinone, propyl gallate, saccharose, 3,5-di-tertbutyl-4-hydroxy-benzylthio glycolate, p-cumaric alcohol, 4-hydroxy-phenylethyl alcohol, coniferyl alcohol or allopurinol, 3,3'-thiodipropionic acid, fumaric acid, dihydroxy maleic acid or edetic acid;
Tb1 = (CO)tx or (X)txx;
C1 = Tc-Y;
t, t', tx, txx = 0 or 1;
Tb = (CO) or X;
X2 = a bivalent group such that the free valences of Tb1 and Tb are saturated with OZ, Z or N(ZI)ZII);
Z, ZI, ZII = H or 1-10C alkyl, preferably 1-5C alkyl;
Tc = CO (when tx = 0) or X (when txx = 0) and ba and ca are 1, or
Tc = CO (when t = 0) or X (when t' = 0) and ba = 0;
Y = rYp, Ya or Yar;
Yp = (C)n1x(Rt1x)(Rt1x')-Y3-(C)-n11x(Rt11x)(Rt1x')-O;
n1x = 0-5 (preferably 1);
n11x = 1-5 (preferably 1);
Rt1x, Rt1x', Rt11x, Rt11x' = H or 1-4C alkyl;
Y3 = 5- or 6-membered heterocyclyl containing 1-3 N, O or S heteroatoms;
Ya = R'O or Aa;
Aa = (CH2-CH(ONO2)-CH2-O)nf', (CH2(ONO2)-CH(CH3)-CH2-O)nf', (CH(R1f)-CH2-O)nf or (CH2-CH(R1f)-O)nf;
R1f = H or CH3;
nf' = 1-6 (preferably 1-4);
nf = 1-6 (preferably 2-4);
R' = 1-20 (preferably 2-6)C alkyl or 5-7C cycloalkylene (in which at least one carbon atom is substituted by heteroatoms and the ring can have side chains of R' type);
Yar = Yar1 or Yar2;
Yar1 = a group of formula (i);
Yar2 = a group of formula (ii);
n3 = 0-5, and
n3' = 1-3,
provided that:
(1) ca and ba are not both 0;
(2) when t is 1, t' is 0 and when t' is 1, t is 0;
(3) when tx is 1, then txx is 0 and when txx is 0, then tx is 1, and

(4) when ca is 0, tx is 0 and Tb1 is O.

An INDEPENDENT CLAIM is included for analgesic drugs for the treatment of chronic pain (e.g. neuropathic pain) in combination with NO donor compounds.

ACTIVITY - Analgesic; Antidiabetic.

In a test, four groups of Swiss male mice (20-25 g) each comprising 10 animals, were administered by intraperitoneal injection gabapentin (90 mg/kg) or 1-(aminomethyl)cyclohexane acetic acid 3-(nitro-oxymethyl)phenyl hydrochloride ester (Ia) at a dose of 50 mg/kg in a saline solution. One hour after administration, formalin (10 mu l) was injected in the paw. In the 15 minutes subsequent to formalin administration, for each animal, the number of times it licked its paw was counted. The results were expressed as a percentage ratio between the number of times where the paw licking was observed in the treated animals to that of the control group. The number of paw-licking (%) for the animals treated with gabapentin/(Ia) and control animals were 80/70 and 100, respectively. The results showed that (Ia) was more active than the starting drug inhibiting the paw-licking.

MECHANISM OF ACTION - None given in the source material.

USE - Used for treating chronic pain e.g. neuropathic pain (claimed) and for reducing diabetic neuropathic pain, and complications caused by diabetes (e.g. affecting the blood vessels and renal apparatus).

ADVANTAGE - (I) Have lower side effects and improved activity in the chronic pain treatment both at the central and peripheral nervous system level. (I) can be used in an amount of less than the maximum indicated for the precursor drugs and also at a higher doses considering their very good tolerability. (I) Show a synergistic effect, allowing the use of a lower amount of the analgesic compound.

Dwg.0/0

TECH UPTX: 20030402

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Preparation of (I) comprises e.g. reacting R-COO-Hal with AgNO3 to give R-COO-Y-ONO2 (I').

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Drugs: (I) is used in combination with NO donor compounds. The NO donor compounds contain in the molecule radicals of drugs belonging to the classes of aspirin, ibuprofen, paracetamol, naproxen, diclofenac or flurbiprofen. The analgesic drugs are lamotrigine, topiramate, tiagabime, zonisamide, carbamazepine, felbamate, amineptine, amoxapine, demexiptiline, desipramine, nortriptyline, opipramol, tianeptine, ami-triptyline, butriptyline, clomipramine, dibenzepin, dimetacrine, dothiepin, doxepin, fluacizine, imipramine, iprindole, lofepramine, melitracen, noxiptilin, propi-zepine, protriptyline or trimipramine.

L12 ANSWER 6 OF 7 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2002-291780 [33] WPIDS
CR 2002-257267 [14]
DNC C2002-085622
TI Preparation of a pharmaceutical composition useful for enhancing the action of an agent involves formulating a central or peripheral nervous system agent with a medium containing a solution of nitrous oxide gas and fatty acid or oils.
DC A96 B05
IN MEYER, P J
PA (PITM-N) PITMY INT NV
CYC 96
PI WO 2002005851 A2 20020124 (200233)* EN 37
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR

KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001081415 A 20020130 (200236)
ADT WO 2002005851 A2 WO 2001-ZA99 20010719; AU 2001081415 A AU 2001-81415 20010719
FDT AU 2001081415 A Based on WO 2002005851
PRAI ZA 2000-3643 20000719
AB WO 200205851 A UPAB: 20020610
NOVELTY - Preparation of a pharmaceutical composition involves formulating a central or peripheral nervous system (CPNS) agent with an administration medium containing a solution of nitrous oxide gas in a carrier solvent for the gas and at least one fatty acid or ester or their other derivatives and reaction product of hydrogenated natural oils.

DETAILED DESCRIPTION - Preparation of a pharmaceutical composition comprises formulating a central or peripheral nervous system (CPNS) agent (I) with an administration medium (II) containing a solution of nitrous oxide gas in a carrier solvent for the gas and at least one fatty acid or ester or their other derivatives (III) and the reaction product of hydrogenated natural oils composed largely of ricinoleic acid based oils such as castor oil with ethylene oxide. (I) is selected from compounds acting an CPNS, but excluding coal tar solution and H1-antagonist antihistamine and also excluding anti-inflammatory, analgesic and antipyretic agents. (III) is selected from oleic acid, linoleic acid, alpha -linolenic acid, gamma -linolenic acid, arachidonic acid, eicosapentaenoic acid (C20: 5 omega 3), decosahexaenoic acid (C22: 6 omega 3), ricinoleic acid and their derivatives selected from 1-6C alkyl ester, glycerol-polyethylene glycol ester, or the reaction product of hydrogenated natural oils composed largely of ricinoleic acid (e.g. castor oil with ethylene oxide).

ACTIVITY - Antidepressant; Tranquilizer; Analgesic; antipruritic.

MECHANISM OF ACTION - None given.

USE - For enhancing the action of a pharmaceutical agent (claimed); such as CPNS; in treating afflictions of the animal body affecting CPNS of an animal; in oral formulation useful as an antidepressant to relieve symptoms of depression and anxiety; to treat certain types of pain; in a topical formulation, as an anti-pruritic to relieve itching in patients with certain types of eczema.

ADVANTAGE - The medium containing a solution of nitric oxide gas has the unexpected property that it displays a remarkable ability to enhance the action of known agents affecting CPNS. The composition has no apparent cytotoxicity.

Dwg.0/0

TECH UPTX: 20020524
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The essential fatty acid or its ester comprises a mixture of fatty esters and is preferably constituted by the complex known as vitamin F ethyl ester having a typical fatty acid distribution as follows: less than 16 carbon atoms (0), hexadecenoic acid (8.3%), octadecanoic acid (3.5%), octadecenoic acid (21.7), octadecadienoic acid (34.8), octadecatetradienoic acid (28%), greater than 18 carbon atoms (1.6%), unknown (2.1%). (II) further includes eicosapentaenoic acid (C20: 5omega3) and/or decosahexaenoic acid (C22: 6omega3) as additional long chain fatty acids.

Preferred Solvent: The carrier solvent is water (preferably deionized water) or alcohol, ether, polymer such as polyethylene glycol or an oil preferably an organic oil more preferably an essential oil based on long chain 14-22C fatty acid in the fatty acid and is preferably of natural origin and most preferably a plant oil rich in gamma linolenic acid.

Preferred Agent: (I) is formulated in a liquid presentation and the formulation incorporates as part of (II), water or other liquid solvent

into which the nitric oxide is dissolved, preferably to saturation and the fatty acid or its ester is dissolved or suspended or emulsified along with (I). (I) is selected form following classes of compounds: central nervous system (CNS) stimulants (IV), CNS depressants (V), local anaesthetics (VI) and medicines affecting autonomic functions (VII). (IV) includes central analeptic (preferably amphetamine, dextroamphetamine, methamphetamine, methylphenidate, caffeine, caffeine citrated, caffeine and sodium benzoate, clomipramine, desipramine, ephedrine, imipramine, pemoline, protryptiline,); psycho analeptic (antidepressant) (preferably a) the tricyclic antidepressants selected from amitryptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, nortriptyline, protriptyline, trimipramine; b) the monoamine oxidase inhibitors selected from isocarboxazid, phenelzine, tranylcypromine; and c) other antidepressants selected from burpopion, fluoxetine, fluvoxamine, maprotiline, mitrazapine, moclobemide, nefazodone, paroxetine, setraline, trazodone, venlafaxine; respiratory stimulant (bronchodilators) (preferably albuterol, ephedrine, ethylnorepinephrine, fenoterol, isoproterenol, metaproteronol, terbutaline); hallucinogenic medicine (preferably a) indoleamine hallucinogenics: LSD, DMT, N,N-dimethylamine, psilocybin, b) the following phenethylamines: mescaline, dimethoxymethylamphetamine (DOM), methylenedioxyamphetamine (MDA), MDMA). (V) includes anaesthetics (preferably halothane, isoflurane, enflurane, methoxyflurane, sevoflurane, desflurane, methohexital, thiopental, etomidate, ketamine, propofol); sedatives and hypnotics (preferably alprazolam, brotizolam, chlordiazepoxide, clobazam, clonazepam, clorazepate, demoxepam, diazepam, estazolam, flumazenil, flurazepam, halazepam, lorazepam, midazolam, nitrazepam, nordazepam, oxazepam, prazepam, quazepam, temazepam, traizolam); barbiturates (preferably amobarbital, aprobarbital, butabarbital, butalbital, mephobarbital, methohexital, pentobarbital, phenobarbital, secobarbital, thiopental); non-barbiturates (preferably buspirone, chloral hydrate, chlormezanone, diphenhydramine, doxylamine, ethchlovynol, ethinamate, glutethemide, hydroxyzine, meprobamate, methotrimeprazine, methyprylon, promethazine, propiomazine, propofol, zolpidem, zolpiclone, paraldehyde); anticonvulsant (including anti-epileptics) (preferably acetazolamide, amobarbital, carbamazepine, clobazam, clonazepam, clorazepate, corticotropin, diazepam, divalproex, ethosuximate, ethotoin, felbamate, fosphytoin, **gabapentin**, lorazepam, magnesium sulfate, mephenytoin, mephobarbital, metharbital, methsuximide, nitrazepam, paraldehyde, paramethadione, pentobarbital, phenacemide, phenobarbital, phensuximide, phenytoin, primidone, secobarbital, trimethadione, valproate sodium, valproic acid); tranquilizer including phenothiazine or its derivatives, rauwolfia, diphenylmethane or its derivatives, alkyl diols or their derivatives (preferably a) phenothiazines and derivatives selected from acetophenazine, chlorpromazine, chlorprothixene, flupenthixol, fluphenazine, mesoridazine, methotrimprazine, pericyazine, perphenazine, pipotiazine, prochlorperazine, promazine, thiopropazate, thioproperazine, thioridazine, thiothixene, trifluoperazine, trifluoropromazine, b) other antipsychotics selected from clozapine, fluspirilene, haloperidol, loxapine, molindone, olanzapine, pimozide, risperidone, lithium); centrally acting muscle relaxant (preferably baclofen, carisoprodol, chlorphenesin, chlorzoxazone, cyclobenzaprine, dantrolene, diazepam, lorazepam, metaxalone, methocarbamol, orphenadrine and orphenadrine citrate, phenytoin). (VI) consists of articaine, benzocaine, bupivacaine, chloroprocaine, cocaine, diphenhydramine, etidocaine, lidocaine, mepivacaine, pramoxine, prilocaine, procaine, propoxycaine, and procaine, proraracain, ropivacaine, tetracaine. (VII) includes adrenomimetics (sympathomimetic) (preferably phenylethylamine, epinephrine, norepinephrine, dopamine, dobutamine, colterol, ethyinorepinephrine, isoproterenol, isoetharine, metaproterenol, terbutaline, metaraminol,

clonldine, phen[illegible]rine, tyramine, hydroxyamphetamine, ritodrine, prenalterol, met[illegible]mine, albuterol, amphetamine, methamphetamine, benzphetamine, e[illegible]rine, phenylpropanolamine, mephentermine, phentermine, fenfluramine, pi[illegible]nexedrine, diethylpropion, phenmetrazine, phendimetrazine) [illegible]enolytics (sympatholytic) (preferably phenoxybenzamine [illegible] related haloalkylamines, phentolamine, prazosin, terazosin, doxaz[illegible] trimazosin, indoramine, labetalol, ketanserin, urapidil, alfuzos[illegible] bunazosin, tamsulosin, yohimbine, propanolol, metoprolol, nado[illegible] atenolol, timolol, esmolol, pindolol, acebutolol, labetalol, bopin[illegible]l, oxprenolol, penbutolol, carvedilol, medroxalol, bucindolol, levu[illegible]lol (betagan) glaucoma, metipranolol, bisoprolof, nebivolol, betax[illegible] (betoptic) glaucoma); the cholinomimetics (cholinergics) (p[illegible]ferably acetylcholine, metacholine, carbachol, betanechol, pilocar[illegible]ine, muscarine, arecoline, oxotremorine, ambenonium, domperidone, edro[illegible]nium, edrophonium and atropine, metoclopramide, neostigmine, phy[illegible]igmine, pyridostigmine); the cholinolytic (anticholinergic[illegible]cluding anti-parkinsonism preparations (preferably amantadine, anis[illegible]pine, atropine, scopolamine and related belladonna alkaloids, iprat[illegible]m bromide, benztropine, biperidine, chlorpromazine, clidinium, dicyc[illegible]e, diphenhydramine, ethopropazine, glycopyrollate, homatropine, hyos[illegible]mine, mepenzolate, methantheline, methoctramine, hexahydrosiladifen[illegible]ol, himbacine, tripitamine, methscopolamine, orphenadrine HCl, p[illegible]enzepine, procyclidine, propantheline, scopolamine, thioridazine, tr[illegible]yphenidyl, carbidopa and levodopa, levodopa, pergolide, seleg[illegible]e); ganglion blockers (preferably hexamethonium, trimethaphan, mecam[illegible]lamine); anti-emetics and antivertigo preparations (preferably 5-HT[illegible]antagonists as ondansetron, granisetron, tropisetron, dolasetron, D2/5 [illegible] antagonist as metoclopramide, trimethobezamide, D2 antagonists as p[illegible]nothiazine e.g. chlorpromazine, perphenazine, prochlorperazine, p[illegible]omethazine, thiethylperazine, triflupromazine, D2 antagonists as ben[illegible]midazole derivatives e.g. domperidone, D2 antagonists as butyrophenone [illegible] haloperidol, droperidol, corticosteroids as dexamethasone, meth[illegible]prednisolone, cannabinoids as dronabinol, nabilone, H1 antagonists di[illegible]nhydramine, meclizine, cyclizine, antimuscarinic agents as scopolam[illegible], benztropiane, benzodiazepines as lorazepam, alprazolam, H1 antagonist as dimenhydrinate; decongestants (preferably oxymetazoline, p[illegible]ephrine, xylometazoline); hydroxytryptamine (serotonin) and [illegible]onin antagonists (preferably a) 5-HT agonists selected from bu[illegible]one, ipsaperone, sumatriptan, cisapride, b) 5-HT antagonists selected from methysergide, risperidone, ketanserin, ondansetron, c) 5 HT transport inhibitors selected from fluoxetine, sentraline); anti [illegible]heimers agents (preferably physostigmine, iacrine and lecithin in combin[illegible]ion with tacrine); histamine and antihistaminic agents (preferably 2(m-F[illegible]phenylhistamine), dimaprit, R-alpha-Me-histamine, ethanolamine as [illegible]noxamine **maleate**, clemastinefumurate, diphenhydramine [illegible], dimenhydrinate, ethylenediamine as pyrilamine **maleate**, tripelen[illegible]ine HCl, tripelennamine **citrate**, alkylamine as chlorpheniramine **maleate**, brompheniramine **maleate**, piperazine as hydr[illegible]yzine HCl, Hydroxyzine pamoate, cyclizine HCl, cyclizine lactate, meclizine HCl, phenotiazine as Promethazine HCl, second generation alkyl[illegible]ne as acrivastine, second generation piperazine as cetrizine HCl, pip[illegible]idine as astemizole, levocabastine HCl, loratadine, terfenadine).

L12 ANSWER 7 OF 7 WP[illegible] COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2000-505576 [45] [illegible]PIDS
DNC C2000-151655
TI Polysome for drug delivery comprises a liposome of a binding agent lipid matrix and a medicament polymer complex bound to the matrix.
DC A14 A96 B03 B04 [illegible] D16

IN LAU, J R
PA (SDGS-N) SDG INC
CYC 89
PI WO 2000032167 A1 20000608 (200045)* EN 29
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GH ... IT KE LS LU MC MW NL
OA PT SD SE SL SZ TZ UG ZW
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FI GB GD GE GH GM HR HU ID IL IN IS JP KE ... KP KR KZ LC LK LR LS
LT LU LV MA MD MG MK MN MW MX NO NZ PL PT ... RU SD SE SG SI SK SL
TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000019219 A 20000619 (200045)
ADT WO 2000032167 A1 WO 1999-US27980 19991126; AU 20... 9219 A AU 2000-19219 19991126
FDT AU 2000019219 A Based on WO 2000032167
PRAI US 1998-110338P 19981201
AB WO 200032167 A UPAB: 20000918
NOVELTY - A pharmaceutical polysome comprises a ...some and a binding agent lipid matrix and a medicament-polymer comp... bound to the matrix.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS a... included for:
(1) a composition for delivery of a therape... agent to a target site, comprising:
(a) a therapeutic agent bound to a first re... ve site on a polymer with a plurality of reaction sites; and
(b) a liposome matrix attached to a binding ...nt, which is also bound to a second reactive site in the polymer a... spacer group to prevent the therapeutic agent from interacting d...tly with the matrix; and
(2) a preparative method for the polysome.
ACTIVITY - Drug delivery; nervous system; a... icrobial; virucide; antibacterial.
MECHANISM OF ACTION - None given.
USE - For drug delivery of biogenic primary ...ne neurotransmitters or alternatively cytokines, proteins, hormones, ...nes, hematopoietic growth factors, chemotherapeutics, antimicrobial... ntivirals and/or antibiotics (claimed).
ADVANTAGE - Avoids systemic side effects by ...aining the drug in the matrix until required.
Dwg.0/2
TECH UPTX: 20000918
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred M...ament: The medicament is a biogenic primary amine neurotransmitter and ... particularly selected from 5-hydroxytryptamine hydrochloride, L-beta-3... ihydroxyphenylalanine, 2-(4-imidazole)ethylamine, 1-(3,4-dihydroxypheny... -aminoethanol, gamma-amino-n-butyric acid, 1-(**aminomethyl**)-**cyclohexaneacetic acid** or a cytokine, protein, h...ne, enzyme, hematopoietic growth factor, chemotherap...c, antimicrobial, antiviral and/or antibiotic. The medicament is r...ed with polymer to give 11.5-34.7 wt.% polymer in relation to the t... lipid weight, particularly in a mole ratio of 3:1 with the ami... edicament.
Preferred Lipid: The lipid is selected from dist...yl-sn-glycerol-3-phosphocholine, cholesterol, a dicetyl phosphate ...or chromium-bis-(N-(2,6-diisopropyl-phenylcarbamylm... l)iminodiacetic acid) especially a mixture of 68.2 wt.% distearoyl-sn-...erol-3-phosphocholine, 8.97 wt.% cholesterol, 17.4 wt.% dicetyl phospha... and 1.18 wt.% chromium-bis-(N-(2,6-diisopropyl-phenylcarbamylm... l)iminodiacetic acid).
Preferred Polymer: The polymer is particularly a...y(**maleic** anhydride-1-octadecene) copolymer.
Preferred Binding Agent: The binding agent is pa...ularly phosphatidyl ethanolamine.

TECHNOLOGY FOCUS - POLYMERS - Preferred Polymer: The polymer is particularly a poly(**maleic** anhydride-1-octadecene) copolymer.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: The polysome is prepared by reaction of a medicament with a polymer having a plurality of reactive sites and further reacting this medicament bound polymer with a binding agent linked to a lipid matrix to bind the matrix to a second binding site on the polymer.

=>

=> fil medline
FILE 'MEDLINE' ENTERED AT 14:53:22 ON 28 OCT 2004

FILE LAST UPDATED: 27 OCT 2004 (20041027/UP). FILE COVERS 1950 TO DATE.

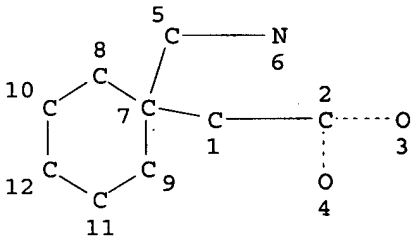
On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD for details.

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que l9
L5 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE
L6 26 SEA FILE=REGISTRY FAM FUL L5
L7 1625 SEA FILE=MEDLINE ABB=ON PLU=ON L6 OR GABAPENTIN
L8 2512 SEA FILE=MEDLINE ABB=ON PLU=ON TARTARIC OR MALEIC OR ETHANEDISULFONIC
L9 0 SEA FILE=MEDLINE ABB=ON PLU=ON L7 AND L8

=> d que l10
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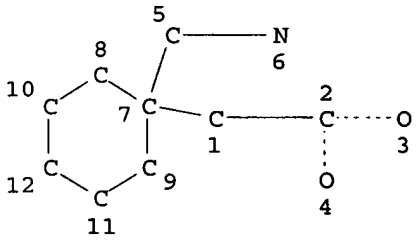

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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE
L6 26 SEA FILE=REGISTRY FAM FUL L5
L7 1625 SEA FILE=MEDLINE ABB=ON PLU=ON L6 OR GABAPENTIN
L10 1 SEA FILE=MEDLINE ABB=ON PLU=ON L7 (L) SALT#

=> d all l10

L10 ANSWER 1 OF 1 MEDLINE on STN
AN 2002465309 MEDLINE
DN PubMed ID: 12224444
TI Gateways to clinical trials.
AU Bayes M; Rabasseda X; Prous J R
Mbayes@prous.com
SO Methods and findings in experimental and clinical pharmacology, (2002 Jul-Aug) 24 (6) 371-91.
Journal code: 7909595. ISSN: 0379-0355.
CY Spain
DT Bibliography
LA English
FS Priority Journals
EM 200305
ED Entered STN: 20020913
Last Updated on STN: 20030503
Entered Medline: 20030502
AB Gateways to Clinical Trials is a guide to the most recent clinical trials in current literature and congresses. The data in the following tables has been retrieved from the Clinical Studies knowledge area of Prous Science Integrity, the drug discovery and development portal, http://integrity.prous.com. This issue focuses on the following selection of drugs: Aciclovir, alemtuzumab, alendronic acid sodium **salt**, alicaforsen sodium, alteplase, amifostine hydrate, antithymocyte globulin (equine), aspirin, atorvastatin calcium, azathioprine; Bacillus Calmette-Guerin, basiliximab, bicalutamide, bimatoprost, BMS-214662, brimonidine tartrate, buprenorphine hydrochloride; Cabergoline, carbamazepine, carboplatin, ciclosporine, cisplatin, cyclophosphamide; Daclizumab, desmopressin acetate, dihydroergotamine mesylate, dorzolamide hydrochloride, doxorubicin, dutasteride; Everolimus; Fluocinolone acetonide, frovatriptan, FTY-720, fulvestrant; **Gabapentin**, galantamine hydrobromide, ganciclovir, gemcitabine, glatiramer acetate; Hydrocodone bitartrate; Interferon beta, interferon beta-1a, interferon beta-1b, ipratropium bromide; Ketotifen; Lamivudine, latanoprost, levodopa, lidocaine hydrochloride, lonafarnib; Metformin hydrochloride, methylprednisolone, metoclopramide hydrochloride, mirtazapine, mitoxantrone hydrochloride, modafinil, muromonab-CD3, mycophenolate mofetil; NS-2330; Olopatadine hydrochloride, omalizumab, oxcarbazepine, oxycodone hydrochloride; Paclitaxel, paracetamol, piribedil, pramipexole hydrochloride, pravastatin sodium, prednisone; Quetiapine fumarate; Raloxifene hydrochloride, rituximab, rizatriptan sulfate, Ro-63-8695, ropinirole hydrochloride, rosiglitazone maleate; Simvastatin, siplizumab, sirolimus; Tacrolimus, tegaserod maleate, timolol maleate, tiotropium bromide, tipifarnib, tizanidine hydrochloride, tolterodine tartrate,

topiramate, travoprost; Unoprostone isopropyl ester; Valganciclovir hydrochloride, visilizumab; Zidovudine.
CT Check Tags: Human
*Drug Therapy
*Randomized Controlled Trials

=>

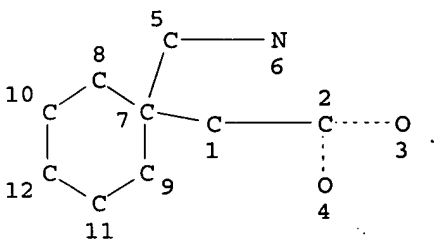
=> fil biosis
FILE 'BIOSIS' ENTERED AT 14:54:29 ON 28 OCT 2004

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 27 October 2004 (20041027/ED)

FILE RELOADED: 19 October 2003.

=> d que l15
L5 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE
L6 26 SEA FILE=REGISTRY FAM FUL L5
L13 1721 SEA FILE=BIOSIS ABB=ON PLU=ON L6 AND GABAPENTIN
L14 4319 SEA FILE=BIOSIS ABB=ON PLU=ON TARTARIC OR MALEIC OR ETHANEDIS
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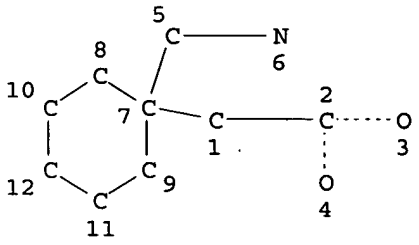

NODE ATTRIBUTES:
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NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE
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L13 1721 SEA FILE=BIOSIS ABB=ON PLU=ON L6 AND GABAPENTIN
L16 1 SEA FILE=BIOSIS ABB=ON PLU=ON L13 (L) SALT#

=> d all l16

L16 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2004:98505 BIOSIS
DN PREV200400096295
TI Solid form investigation of the zwitterion histidine and its **salts**

AU Johnson, M. N. [Reprint Author]; Feeder, N.; Snowden, M. J. [Reprint Author]; Mitchell, J. [Reprint Author]
CS University of Greenwich, Anson, Chatham Maritime, Medway Campus, Kent, ME4 4TB, UK
SO Journal of Pharmacy and Pharmacology, (September 2003) Vol. 55, No. Supplement, pp. S.6. print.
Meeting Info.: Science Proceedings of the British Pharmaceutical Conference. Harrogate, England, UK. September 15-17, 2003.
CODEN: JPPMAB. ISSN: 0022-3573.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 18 Feb 2004
Last Updated on STN: 18 Feb 2004
CC General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Pharmacology - General 22002
Pharmacology - Neuropharmacology 22024
IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques; Pharmacology
IT Chemicals & Biochemicals
gabapentin [neurontin]: anticonvulsant-drug; zwitterion histidine: solid form characteristics; zwitterion histidine **salts**: solid form characteristics

IT Methods & Equipment
Cambridge Structural Database [CSD]: computer software; DSC [differential scanning calorimetry]: laboratory techniques, spectrum analysis techniques; Raman spectroscopy: laboratory techniques, spectrum analysis techniques; SEM [scanning electron microscopy]: imaging and microscopy techniques, laboratory techniques; TGA: laboratory techniques; dynamic vapor solution: laboratory techniques; isothermal microcalorimetry: laboratory techniques; light microscopy: imaging and microscopy techniques, laboratory techniques; powder X-ray diffraction: laboratory techniques, spectrum analysis techniques

RN **60142-96-3 (gabapentin)**
60142-96-3 (neurontin)

=>